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Relationships Between Questionnaire Responses and Children's Pesticide Exposure Measurements

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Relationships Between Questionnaire Responses and Children's Pesticide Exposure Measurements

by

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Executive Summary

Children are widely acknowledged to be more vulnerable than adults to many environmental health hazards, including pesticides, because they are more exposed, and because they may have elevated susceptibility. The effect of relatively low levels of pesticide exposure in children is an area of great scientific uncertainty and has, therefore, become the focus of substantial research and regulatory activities. The work of the Pesticides in Young Children Border States Program to identify the major exposure risk factors for intervention requires studying children across the exposure measurement distribution, especially those with higher exposure measurements. Questions that could be used for exposure classification as a prescreening tool would help produce either an enriched population (i.e., a larger percentage of individuals with higher exposure levels) or would eliminate individuals with lower exposure levels from further review. Considerable savings in time and money may then be realized in selecting the desired population for a study.

The objective of this project is to identify questions that indicate a higher likelihood of predicting a child's level of exposure to pesticides as input to future study designs. This report reviews the state of the science in relating questionnaire responses to environmental and biological measurements, primarily for children, based on results and data from previous exposure studies. A two-part approach was used for this evaluation:

- A literature review of previous exposure studies to summarize the existence of such quantitative and qualitative relationships, and
- An analysis of Phase II of the Pesticide Exposure and Health Effects on Children Initiative (Yuma Study), which contained questionnaires and measurements.

The literature review of previous exposure studies identified 20 publications that met the criteria set for this evaluation. These publications were reviewed in detail to determine the relationships that were considered and statistically analyzed in each study. Relationship, as used here, is defined as a systematic correspondence between the values of two variables, that is, questionnaire responses and analytical measurements. Detailed information about each relationship was compiled to allow for more in-depth evaluations by other researchers as their interests dictated. The questions were grouped into categories for evaluation, and questions showing overall significance across the publications were identified.

From the 20 relevant publications, 603 statistically significant and non-significant relationships across 117 questions in 14 question categories were identified. Eighty-six percent of the relationships were in the categories of residential pesticide use, household characteristics, household occupation, residential proximity to agricultural fields, subject's personal characteristics, and family hygienic practices. These six categories represent questions whose relationships with exposure measurements have both a strong theoretical basis and the quality of being reasonably evaluated through the study designs. Sixty-six percent of the relationships considered metabolites in urine measurements, primarily with DAP-based metabolites, and 31 percent of the relationships considered dust measurements. Three risk factors related to the take-home or para-occupational exposure pathways were analyzed as separate question categories: household occupation, family hygiene practices, and work exposure/practices.

The relationships for each question and chemical/metabolite combination were reviewed to determine the question's effectiveness for differentiating exposure levels. Generally the questions showing the most effectiveness were:

- residential pesticide use (inside and outside)
- occupation of household members
- child's characteristics (age, ethnicity, family income)
- family hygiene practices.

Several other questions, which were tested less extensively in the publications, also showed some effectiveness:

- pets
- household location: urban vs non-urban
- dietary behaviors (organic food)
- exposure levels of household members
- health status (diseases)
- smoking behaviors
- proximity to agricultural fields (for house dust only).

The Yuma Study was conducted from October 1999 through February 2000 for 152 households of permanent residents of the area with children in kindergarten or first grade. The children's urine samples were measured for the six most common dialkylphosphates (DAPs) associated with OP pesticides. Dust samples collected from each household and from classrooms were measured for specific organophosphorous (OP), organochlorine, pyrethroid, and carbamate pesticides. One set of statistical analyses considered the urine, dust, and questionnaire data to identify any associations between questionnaire data and pesticide exposure levels. Traditional statistical techniques were performed to test predefined hypotheses on the principal participant children and their siblings between 2 and 11 years of age. Of the questions analyzed, recent indoor pesticide use, household members working in agriculture, and distance from home to agricultural fields have statistically significant relationships with the ethylated DAP sum and with individual ethyl and methyl DAPs; however, the direction of some relationships was opposite of what might be expected.

A second set of statistical analyses was performed only on principal participant children from the eight schools and two grades in the initial study design. A data mining approach, Classification and Regression Trees (CART), was used to identify potential predictors without specifying a priori hypotheses between the biomarker measurements and the questions and dust measurements. Six scenarios with increasing levels of measurement burden from questions, household dust, and school dust were analyzed for the ethylated and methylated DAPs sums.

Although there are differences in the subpopulations considered and the statistical analyses performed, a summary of the questions selected under either approach for both DAP sums provides a view of the effective differentiators from the Yuma Study. The best use of these results is as "indicators" of predictors that are more useful in differentiating the exposure levels.

Table ES-1 Comparison of Questions Selected from the Yuma Study for the Sum of Methylated and Ethylated DAPs Based on Two Analysis Approaches

Sum of Methylated DAPs	Sum of Ethylated DAPs
	Recent use of pesticides inside home
Child's characteristics (height, weight)	Child's characteristics (weight, ethnicity)
	Other adult in household working in agriculture
Proximity to agricultural fields, spraying conditions	Proximity to agricultural fields, spraying conditions
	Child's time spent away from home
Where in house child spends time	
Child's school	
Father's occupation	
	Diet - local fruits/vegetables

Questions that seem to have stronger relationships with the exposure levels across both the literature review and the Yuma Study include the following:

- occupation of adults living in household
- residential pesticide use
- residential proximity to spraying and agricultural fields
- characteristics of the subject that may indicate potential exposure activities
- family hygiene practices that may mitigate the take-home pathway exposure
- where the child spends time (in home, away from home)
- diet with respect to locally-grown fresh fruits and vegetables.

This report reviews the state of the science in relating questionnaire responses to environmental and biological measurements primarily for children. Future studies that use biological monitoring and questionnaires should draw upon this and other recent research to refine study protocols with the following recommendations.

Based on the literature review, 41 questions were identified as effective in differentiating exposure levels of at least one chemical/metabolite in urine and dust measurements. These questions are offered as a resource of recommended questions with specific chemicals or metabolites for future study designs. Note that the questions were evaluated here as a screening tool to create an enriched population of participants with higher exposure levels. Thus, their future use is better suited to similar purposes.

Table ES-2 Questions Considered Effective Differentiators of Children's Pesticide Exposure Levels (Extracted from Table 2.11)

Medium		Q Category	Q Description
Urine	Dust		
		Residential Pesticide Use	
X			Were the "bedrooms" in the house treated with pesticides?
X			Were the "closets" in the house treated with pesticides?
X			Was the "dining room" in the house treated with pesticides?
X			Was the "living room" in the house treated with pesticides?
X			Was an "other room" in the house treated with pesticides?
X	X		Was the outside of the house treated with pesticides?
X			Was the garden treated with pesticides?
X			Was the lawn or yard treated with pesticides?
X			Level of household pesticide use
X			Number of times personally applied pesticides inside the house
X			Number of times personally applied pesticides outside the house
X			Was the inside or outside of the house treated with pesticides by a family member?
X			Did you personally mix pesticide inside the house?
		Household characteristics	
	X		Is the property used as a farm?
	X		Number of persons living in household
X			Do you have pets in the house?
X			Do you have pets inside or outside the house?
X			Does household have a garden or vegetable garden?
		Household occupation	
	X		Number of agricultural workers in household
	X		Applicator vs farm worker
	X		Applicator vs non-applicator
X	X		Applicator and farm worker vs reference
X			Applicator vs reference
	X		Fieldworker vs pesticide handler
X			Did head of household spray fields?
X			Was a household member recently involved in fieldwork?

Medium		Q Category	Q Description
Urine	Dust		
	X		Are household members involved in tree thinning?
	X		Number of household members with high pesticide contact jobs
		Residential proximity to agricultural fields	
X	X		Proximity of home to pesticide-treated farmland/orchard
		Residential location	
X			Urban vs non-urban
		Subject's personal characteristics	
X			Age
X			Ethnicity
X			Income
		Child's behaviors	
X			Hand wipe concentration per unit area
		Dietary behaviors	
X			Was diet conventional or organic?
		Family hygiene practices	
	X		Are work clothes worn inside the house?
	X		Number of weeks since last house was last vacuumed
		Related exposure levels	
X			Number of adult household members with high metabolite levels
		Health	
X			Have you ever had bowel disease?
X			Have you ever had intestinal disease?
X			Have you ever had ulcers?

Analyses of the association between questionnaire data and pesticide metabolites in children's urine are conducted on the assumption that the urinary metabolite measurements provide an accurate estimate of children's exposure. Metabolites under study are processed and excreted relatively quickly in humans (1-3 days), which is in contrast to the general nature, in terms of the time frame of a particular activity or behavior, of most questions asked of parents or children. It is therefore worthwhile to consider the variability in measurements in urinary pesticide metabolites. Recent studies suggest that if complete 24- or 48-hour urine samples are collected rather than spot urine samples, it may be possible to better identify major risk factors for exposure.

Validity of questionnaire data is an essential consideration in epidemiologic studies, and future studies of children's pesticide exposure should be preceded by validation studies. Such studies might include validating the basis for classifying each applicator's exposure through biological monitoring, or evaluating the correlations between self-reported behavioral data from potential participants and the urinary metabolite data.

Studies of children's pesticide exposure should work to improve the quality of data related to behavior. At present, researchers rely primarily on parental reports of behavior for young children. Yet the validity of parental reports has not been scrutinized in a systematic fashion. There is clearly a need for more objective measures of children's activities and behaviors in conjunction with systematic biological monitoring to ensure identification of key predictors of children's exposure to pesticides.

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Abstract

Children are deemed to be more vulnerable than adults to many environmental health hazards, including pesticides, and the effect of relatively low levels of pesticide exposure in children has become the focus of substantial research and regulatory activities. To identify the major exposure risk factors for intervention, the Pesticides in Young Children Border States Program requires studying children across the exposure measurement distribution, especially those with higher exposure measurements. Questions that could be used for exposure classification as a pre-screening tool may prove to be a cost-effective way to select the desired population for a study. A two-part approach was implemented to identify questions that indicate a higher likelihood of predicting a child's level of exposure to pesticides as input to future study designs:

- A literature review of previous exposure studies to evaluate questions used, and
- An analysis of a recent children's pesticide exposure study.

From the 20 relevant exposure study publications, 603 relationships, statistically significant and not, across 117 questions in 14 question categories were identified. The relationships for each question and chemical/metabolite combination were reviewed to determine the question's effectiveness for differentiating exposure levels. Generally the questions showing the most effectiveness were: residential pesticide use (inside and outside), occupation of household members, child's characteristics (age, ethnicity, income, and family hygienic practices. Several other questions, which were used less extensively in the studies, also showed some effectiveness.

Data from a recent study of children's exposure to pesticides conducted in Yuma, Arizona, was analyzed from two perspectives: traditional statistical analyses on predefined hypotheses of potential risk factors, and a data mining approach to explore the relationships existing in the data. Both analyses evaluated the relationships between the dialkylphosphate (organophosphate pesticide) metabolite levels in the children's urine samples, the pesticide levels in the household and school dust samples, and the questionnaire responses.

Questions that seem to have stronger relationships with the exposure levels across both the literature review and the analysis of the exposure study include the following: occupation of adults living in household, residential pesticide use, residential proximity to spraying and agricultural fields, characteristics of the subject that may indicate potential exposure activities, family hygienic practices that may mitigate the take home pathway exposure, where the child spends time (in home, away from home), and diet with respect to locally-grown fresh fruits and vegetables.

This report reviews the state of the science in relating questionnaire responses to environmental and biological measurements, primarily for children. Future studies that use biological monitoring and questionnaires should draw upon this and other recent research to refine study protocols with the recommendations noted.

Acknowledgements

No large project like this report is accomplished by the co-authors alone, and we would like to gratefully acknowledge those who helped in this process. Andy Tsang, Anteon Corporation, helped with some of the statistical analyses and facilitated the transition of the relationship database entries for the tables in Appendices B, C, and D. Dr. Peter Stephan, Anteon Corporation, was responsible for the technical preparation of the document, which included valuable comments for making the information-intensive tables more readable. Guadalupe Chapa, Fellow of Associated Schools of Public Health, provided comments and clarifications. Thank you.

None of this work would be possible without the continued commitment of the researchers focused on children's exposure to pesticides, both through the publications we reviewed and their willingness to answer questions related to their work. There are many other researchers in this area whose work, though not directly relevant to this report, is part of the set of building blocks upon which this area of research depends. We hope that those engaged in this field find the results of this work useful in their future research efforts. Finally, we gratefully acknowledge all of the families who have participated in these studies; without their cooperation we would not be able to progress in our understanding of these important issues.

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Figures

1.0 INTRODUCTION

1.1 Introduction

The Pesticides in Young Children Border States Program (USEPA 2002) includes a series of studies designed to develop and implement an approach for examining the cumulative risks and potential health effects in children from repeated exposure to pesticides via multiple sources and pathways. The work of this program includes identifying the major exposure risk factors for intervention that require studying the full range of the exposure measurement distribution for children, especially for children with high exposure measurements. Various screening processes have been studied to help identify populations of interest. This report presents an evaluation of questions and environmental measures used in previous exposure studies as potential indicators of pesticide exposure (e.g., metabolite levels in children's urine).

1.2 Children's Exposure to Pesticides

Pesticides represent a wide range of chemicals that are used in agricultural production, vector control, and food preservation, as well as in residential environments for aesthetic and pest control purposes. Many pesticides currently registered in the United States have documented health effects, including acute toxicity and carcinogenicity. The effect of relatively low levels of pesticide exposure in children is an area of great scientific uncertainty, and has, therefore, become the focus of substantial research and regulatory activities. It is widely acknowledged that children are more vulnerable to many environmental health hazards than adults, including pesticides, because they are more exposed and because they may have elevated susceptibility (Needham and Sexton 2000).

The 1993 National Academy of Sciences report, *Pesticides in the Diets of Infants and Children*, highlighted this concern, and pointed out the complexities involved in the evaluation of aggregate exposures and cumulative risks (NRC 1993). The Food Quality Protection Act (FQPA) of 1996 called upon the U.S. Environmental Protection Agency (U.S. EPA) to implement risk assessment procedures that would be protective of children in their dietary exposures to pesticides, and that would factor in exposures from other sources, such as residential pesticide use (http://www.epa.gov/opppsps1/fqpa/).

The last decade has seen a substantial increase in studies aimed at characterizing children's exposure to pesticides. The U.S. EPA Science to Achieve Results (STAR) grant program (http://www.epa.gov/ncer/grants/), established in 1996, has provided an ongoing source of funds that are distributed to investigators throughout the country, based on peer review of proposed projects for scientific excellence. Several of the STAR grant programs have addressed children's exposure to pesticides (http://www.epa.gov/ncer/grants/ and USEPA 1997). A substantial research program on children's pesticide exposure (USEPA 2000b, USEPA 2003) has also been developed within the Agency, and in conjunction with other federal agencies, such as the Centers for Disease Control and Prevention (CDC). The work produced by these studies affords the first opportunity to evaluate systematically the effectiveness of particular exposure assessment methods.

1.3 Populations of Concern

Recent studies (Aprea 2000, Lu 2001, Adgate 2001, Curl 2003, Heudorf 2004, Morgan 2004) have tended to focus on relatively young children – either pre-school or elementary school age. It is believed that such children may be at greater risk, both in terms of exposure and susceptibility. Several sub-groups of children have been studied because they were believed to be at particularly high risk. For example, numerous studies (Koch 2002, Shalat 2003, Fenske 2002, Royster 2002) have focused on children in agricultural communities due to the high use rates of pesticides in and around these communities. Children of minority or disadvantaged groups have also been examined (Mills and Zahm 2001, Grossman 2001, Krinsley 1998, McCauley 2001, Quandt 2004) as part of a broader environmental justice initiative within the federal government. Finally, children whose parents are exposed to pesticides in the workplace have received special attention (Loewenherz 1997, Lu 2000, Azaroff 1999, Curl 2002), as it is well documented that workplace contaminants can contribute to the exposure of children. Participant recruitment strategies for these studies have ranged from convenience to probability-based sampling approaches.

1.4 Exposure Pathways and Patterns

Children's exposure to pesticides typically involves multiple pathways and multiple routes as shown in Figure 1.1, which is adapted from Cohen Hubal (2000a) and Cohen Hubal (2000b).

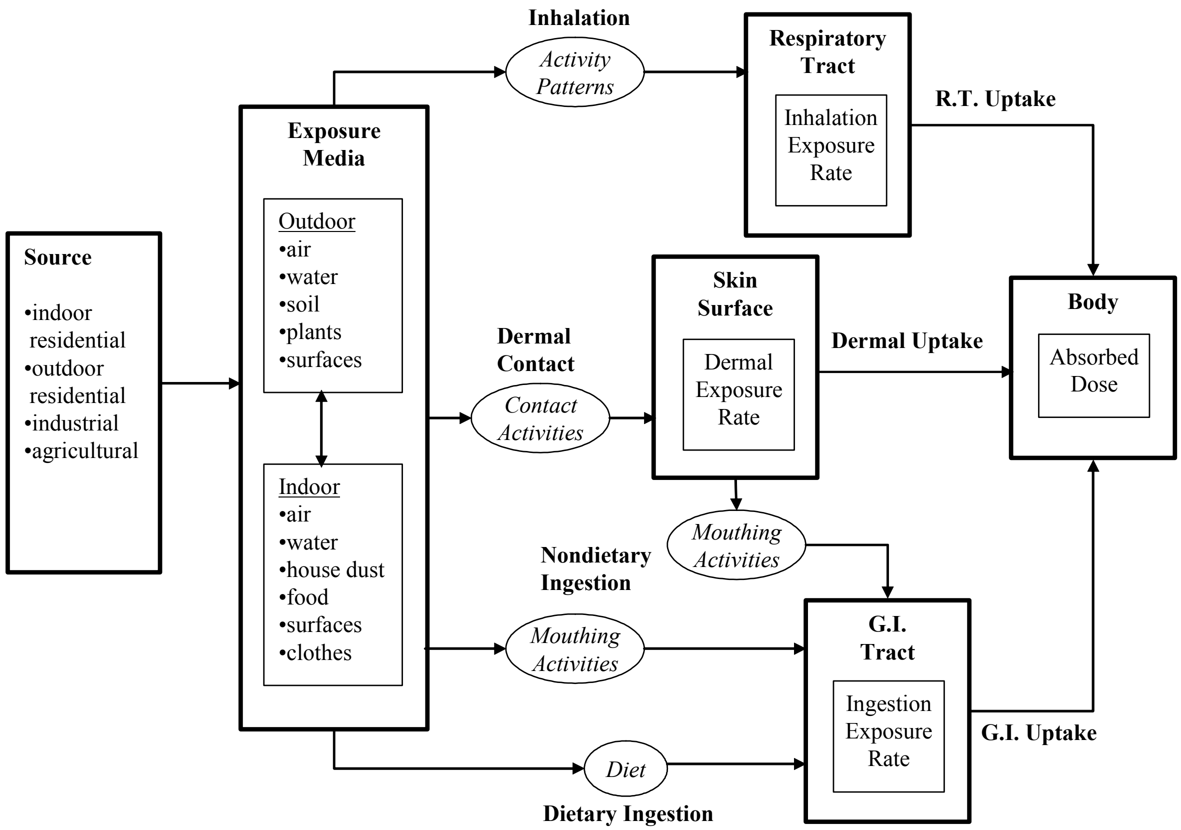

Figure 1.1 Activities, Pathways, and Routes Related to a Child's Exposure to Pesticides
(adapted from Cohen Hubal 2000a and Cohen Hubal 2000b)

Although most of the pathways and routes for children are similar to those for adults, the types of, and amount of time spent at, activities will differ from adults, and between children of different ages. As a result, the assessment of such exposures is among the most challenging tasks faced by exposure assessment scientists. In addition to exposure from diet and drinking water, children naturally explore their environment. Contact with surfaces, frequent mouthing activities, and even the consumption of soil or dust can contribute to exposures, and the temporal and spatial patterns of these exposures can be unpredictable (Black 2005).

1.5 Questionnaire Data

Questionnaires have long been used as a primary source of exposure data in epidemiologic studies. Most epidemiologic investigations are initiated after exposure has begun, and structured interviews or questionnaires are used to reconstruct historical exposure patterns. Such an approach raises questions regarding recall accuracy and possible bias (Teitelbaum 2002).

In contrast, contemporaneous studies of children's pesticide exposure often include some type of exposure measurement. In such study designs, questionnaires are generally used to identify important risk factors or exposure pathways. The exposure measurements are usually considered objective measures of exposure and are treated statistically as outcome variables. Questionnaire data are more easily collected than environmental measurements and are, therefore, more cost-effective. In large population studies questionnaires may be the only means available to ascertain exposure information. Yet questionnaires carry with them some important limitations. Questions are often posed in very general terms (e.g., "ever/never") and so fail to specify the temporal pattern of the exposure. Questions may also lack specificity in regard to behavior (e.g., does a child practice hand-to-mouth behavior), so that the frequency of the behavior remains unknown. While many researchers have attempted to address these limitations, there is also a limit to the number of questions that can be posed and the level of detail that can be requested before study participants become reluctant or unable to continue with the study.

Two large-scale research endeavors have made great strides in the development and use of questionnaires in exposure assessment and epidemiology. First, the National Human Exposure Assessment Survey (NHEXAS) (Sexton 1995b) was developed by the U.S. EPA with the specific goal of improving the quality of exposure data. Studies sponsored under this program have included probability-based subject recruitment, carefully tested questionnaires and diaries, and accompanying environmental measurements for a variety of environmental contaminants including pesticides. Second, the Agricultural Health Study (http://www.aghealth.org), led by the National Cancer Institute (NCI), has incorporated a prospective study design, using questionnaires at the outset of the study, and periodically throughout the life of the study. NCI has also worked collaboratively with U.S. EPA to examine the validity of questionnaire responses through the collection of exposure measurements (Dosemeci 2002). These studies are likely to add significant new knowledge to the field of exposure assessment.

1.6 Exposure Measurements

Measurements used in studies of children's exposure to pesticides have focused primarily on samples collected in the children's microenvironments (e.g., homes, daycare centers, special play areas). Sampling media have included soil, house dust, and wipes of surfaces. The hands of children have also been washed or wiped to provide a relative indicator of dermal exposure. An important feature of many of these studies has been the quantitation of children's behavior (e.g., frequency of hand-to-mouth contact), although most data on behavior have been collected in studies that have not included exposure measurements (Cohen Hubal 2000b). Finally, biological exposure methods have been used to evaluate pesticide exposure (Barr 1999, Barr and Needham 2002). Urine sampling has been used most frequently in studies of children's exposure, as it does not involve invasive sampling. Saliva monitoring of pesticides has proven feasible in animal models (Lu 2003). Current studies include the collection and analysis of saliva samples from young children in an effort to measure pesticides directly rather than as metabolic byproducts (www.sph.emory.edu/eoh/faculty/Lu.html).

Environmental and biological samples are considered objective measures of exposure, and they are sometimes viewed as representing a kind of "gold standard" when compared with questionnaire data. However, these measurements can have substantial analytic variability. For example, house dust is a complex matrix that may vary from location to location within a residence. Extraction procedures may produce a range of values for the same measured sample. Metabolites in urine may require derivatization before analysis, a step that can introduce variability in the analytical results.

Furthermore, exposure measurements can vary over time. This is most pronounced in the case of spot urine samples collected to measure exposure to pesticides that are rapidly excreted (1-3 days). Significant variability can be observed day to day for the same individual as well as for a group of individuals whose exposures are presumably the same. Thus, it is important to consider both the quality and the potential for variability in exposure measurements when assessing the utility of questionnaire data in predicting exposure levels.

1.7 Border States Program: Pesticides in Young Children

Research for the Pesticides in Young Children Border States Program is being, and has been, conducted in the U.S.-Mexico Border States of Arizona, California, New Mexico, and Texas as part of the Environmental Health Workgroup on the U.S.-Mexico Border program (http://www.epa.gov/orsearth) which was developed with the passage of the North American Free Trade Agreement (NAFTA). A three-phase approach was undertaken to address the project objectives. Phase I was a planning phase. It included a review of existing environmental pesticide exposure and health data, and the identification/review of techniques for measuring pesticides and pesticide biomarkers in environmental and biological media Phase II evaluated the extent and distribution of pesticide exposure in children living in the border region with the intent of identifying those children with the highest levels of exposure. Phase II also included methods development and evaluation studies to fill data gaps needed for the design of Phase III. The initial Phase II analyses suggest that the existing Phase II studies have not identified a definitive population for the Phase III activities.

The planned Phase IIIa would include a more complete monitoring of children classified in Phase II as "high end exposures." Follow-up on these children would include detailed measurements of their environmental exposure and biological monitoring for levels of metabolites. From the Phase IIIa effort, a study would be designed to evaluate the relationships between pesticide exposures and selected health outcomes and to define specific hypotheses to be tested. An epidemiological study (Phase IIIb) may then be performed to examine the specific hypotheses about the impact of pesticide exposure on health status/outcome of children. In order for the Pesticides in Young Children Border States Program to move towards the Phase III goals, better exposure classification tools are needed to identify a subset of children likely to have higher exposure levels so that a Phase IIIa study can be performed in a cost effective manner.

1.8 Motivation and Goal of the Project

The current goal of many exposure assessment studies is to collect information using questionnaires and diaries, environmental measurements and biomarkers, to develop an understanding of the levels of chemicals to which people are exposed and to understand how these exposures might occur. This approach is useful when the objective of the study is to determine the population distribution of exposure to a chemical. A different approach is needed; however, when the objective is to identify those individuals with higher exposure levels for intervention and additional study. In many exposure assessment studies, the chemical/metabolite levels from most of the participants are either not detectable or below the level of concern for the chemical of interest. Thus, a large proportion of the available funding for a study may be used to collect data that has little value in identifying and subsequently protecting the most highly exposed individuals. Since the collection and analysis of environmental and biological samples is an expensive portion of the exposure evaluation process, considerable savings in time and money may be realized if questionnaires could be used in an effective manner to predict those individuals with higher exposure levels.

Because of the potential reduced costs and other benefits, the Pesticides in Young Children Border States Program would like to employ questionnaires in the Phase IIIa study for exposure classification to aid in selecting the desired population for study. This selection would produce either an enriched population (i.e., a larger percentage of individuals with higher exposure levels) or would eliminate from further analysis individuals with lower exposure levels. These interests require having questions that can predict the likelihood that an individual has been exposed to pesticides.

1.9 General Approach and Report Contents

The work presented in this report offers researchers another tool for selecting the questions to be included in a study's design. In some studies, experts using a Delphi consensus process (http://www.scu.edu.au/schools/gcm/ar/arp/delphi.html) to consider hypothetical and observed relationships described in the research literature that are pertinent to the study's interests. This report reviews the state of the science in terms of how well questionnaire responses, from previous exposure studies, are statistically related to environmental and biological measurements for children. The approach for evaluating these relationships was twofold, and includes:

- A literature review of previous exposure studies to summarize the existence of such quantitative and qualitative relationships, and
- An analysis of a recent children's pesticide exposure study in Yuma, Arizona, which included questionnaires and measurements.

Section 2 of this report provides a summary of this project's results and recommendations for additional work. It describes both the questions and categories of questions that were found to be the most useful in differentiating children's pesticide exposure levels to pesticides in the context of future study designs. Section 3 describes the methodology used for the literature review and the statistical analysis of the Yuma study data. Section 4 includes details of the results from the literature review and from the Yuma Study data. Section 5 lists the references cited in this report. Appendix A lists the publications included in the literature review. Appendices B, C, and D present the overview, detail, and comments tables describing the relationships between questionnaire responses and pesticide exposure measurements extracted from the literature review, as summarized in Section 4. Appendix E describes the questions for which relationships from the literature review were tracked. Appendix F lists the chemicals used in the Yuma Study analyses, and describes the molar weighting process used to create the combinations of the chemicals/metabolites. Appendix G describes the methodology and provides detailed results of the data mining approach for the Yuma Study as summarized in Section 4.

2.0 SUMMARY AND RECOMMENDATIONS

2.1 Introduction

Children are widely acknowledged to be more vulnerable than adults to many environmental health hazards, including pesticides, because they are more exposed, and because they may have elevated susceptibility (Needham and Sexton 2000). The effect of relatively low levels of pesticide exposure in children is an area of great scientific uncertainty and has, therefore, become the focus of substantial research and regulatory activities. The work of the Pesticides in Young Children Border States Program (USEPA 2002) includes identifying the major exposure risk factors for intervention, which requires studying children across the exposure measurement distribution, especially those with higher exposure measurements.

The goal of many exposure assessment studies is to collect information using questionnaires and time-activity diaries, environmental measurements and biomarkers, to develop an understanding of the levels of chemicals to which people are exposed and to understand how the exposures might occur. In the typical exposure assessment study, the measurements from most of the participants are either not detectable or below the level of concern for the chemical of interest; thus, a large proportion of available funding for a study may be spent collecting data that has little value in identifying, and subsequently protecting, the most highly exposed individuals. Considerable savings in time and money may be realized if questionnaires could be used for exposure classification that would aid in selecting the desired population for a study. Such a screening tool would help produce either an enriched population (i.e., a larger percentage of individuals with higher exposure levels) or would eliminate individuals with lower exposure levels from further review.

The objective of this project is to identify questions that indicate a higher likelihood of predicting a child's level of exposure to pesticides as input to future study designs. The work presented in this report reviews how well questionnaire responses, based on previous exposure studies, are statistically related to environmental and biological measurements for children. The approach for evaluating these relationships was twofold, and includes:

- A literature review of previous exposure studies to summarize the existence of such quantitative and qualitative relationships, and
- An analysis of a recent children's pesticide exposure study in Yuma, Arizona, which contained questionnaires and measurements.

This section describes both the questions and categories of questions that were found to be the most useful in differentiating children's pesticide exposure levels to pesticides in the context of future study designs, discusses issues in developing effective screening tools, and includes recommendations for additional work.

2.2 Methods

Questions for a new exposure study design are usually selected based on theoretically-defined or hypothesis-driven relationships, the results of relationships tested in previous exposure studies, and the interests of the new study. Relationship, as used in this report, is defined as a systematic correspondence between the values of two variables, that is, questionnaire responses and analytical measurements. This correspondence may or may not be statistically significant. Some questions or categories of questions become the typical selections for exposure studies because of the results from previous studies. This report reviews the state of the science in relating questionnaire responses to environmental and biological measurements, primarily for children, based on results and data from previous exposure studies. A two-part approach evaluated questions from the studies to identify those showing strong, that is, statistically significant, relationships with pesticide exposure levels.

One part of the approach was based on a literature review of previous exposure studies. A search through several resources identified over 100 citations that might meet the criteria set for this evaluation. The abstracts and full publications, where necessary, were reviewed with respect to the following criteria:

- Was pesticide exposure studied?
- Were relationships between questions and measurements from monitoring, and preferably urine, samples described? and
- Were children included as part of the population studied?

The 20 publications that were selected as being relevant for evaluating the usefulness of questions were reviewed in detail to determine the relationships that were considered and statistically analyzed in each study. A simple MS Excel database was created to track the relationships between questions, and environmental and biological measurements, as noted in the publications, whether or not the statistical tests of the relationships were statistically significant. Detailed information about each relationship was compiled to allow for more in-depth evaluations by researchers as their interests dictated. The questions were grouped into categories for evaluation and questions showing overall significance across the publications were highlighted. It should be noted that the 20 publications represent 14 distinct studies. Details on the publication selection process and the extraction of the relationship information are described in section 4.2.

The second part of the approach reviewed a recent study of children's exposure to pesticides from Phase II of the Pesticide Exposure and Health Effects on Children Initiative (section 1.6). Some analyses had already been performed to meet the study's objectives and were summarized in a report (CDC 2002). Subsequent analyses of the data using a data mining approach were then performed for this project to identify relationships that exist in the data rather than ones that are predetermined by the study's hypotheses. Preliminary bivariate analyses and principal component analyses were performed to fine-tune the analysis approach and to help understand some of the underlying structures within the data. The main type of analysis performed was Classification and Regression Trees (CART). This technique was used to investigate several scenarios of questions and dust measurements as potential predictors for the sum of the ethylated dialkylphosphates (DAPs) and the sum of the methylated DAPs (Appendix F). The questions and dust measurements that were selected as predictors from the CART analysis in more than 50% of the scenarios were identified as useful in differentiating exposure levels.

2.3 Results

2.3.1 Literature Review

Relationships are evaluated as the means for testing a study's hypotheses, and results of these evaluations are included in publications based on the study. From the 20 relevant publications, 603 relationships across 117 questions in 14 question categories were identified. All statistically significant and non-significant relationships were noted except for a large number of non-significant relationships alluded to in Sexton (2003) (section 4.2.2.2). Appendix E lists the questions included under each of the 14 categories.

Table 2.1 Distribution of Questions and Relationships Across 14 Question Categories

Group	Category	# questions[a]	# relationships[b,c]	% relationships	# publications[d]
Source	Residential pesticide use	32	100	16.6	11
Source	Household characteristics	17	73	12.1	7
Source	Residential sources (environmental measurements)	3	13	2.2	4
Source	Household occupation	16	115	19.1	11
Source	Residential proximity to agricultural fields	2	72	11.9	10
Source	Residential location	5	14	2.3	4
Behavior	Subject's personal characteristics	6	78	13.0	9
Behavior	Child's behaviors	6	20	3.3	4
Behavior	Dietary behaviors	4	16	2.7	3
Behavior	Family hygiene practices	11	81	13.4	7
Behavior	Smoking-related activities	3	4	0.7	1
Behavior	Work exposure practices	4	4	0.7	2
Other	Related exposure levels	2	5	0.8	1
Other	Health	6	8	1.3	1
	Total	117	603	100	

[a] See Appendix E for list of questions tracked in the literature review.
[b] # relationships obtained by totaling numbers from tables in Appendix B for each category.
[c] See section 4.2.2.2 regarding relationships from Sexton (2003).
[d] Number of publications from the relevant list that were sources for the relationships.

Eighty-six percent of the relationships were in the categories of residential pesticide use, household characteristics, household occupation, residential proximity to agricultural fields, subject's personal characteristics, and family hygiene practices (Table 2.1). These six categories represent questions whose relationships with exposure measurements have both a strong theoretical basis, and could be reasonably evaluated through the study designs.

Table 2.2 Distribution of Questions and Relationships Across Medium Measured

Medium	# questions[a,b]	# relationships[c,d]	% relationships	# publications[e]
Urine – DAP	47	267	44.3	12
Urine – non-DAP	68	129	21.4	5
Dust	42	187	31.0	8
Indoor Air	2	3	0.5	1
Outdoor air	1	2	0.3	1
Personal air	2	4	0.7	1
Soil	2	8	1.3	1
Solid food	2	3	0.5	1
Total	166[f]	603	100	

[a] See Appendix E for list of questions tracked in the literature review.
[b] Some questions were related to measurements in more than one medium.
[c] See section 4.2.2.2 regarding relationships from Sexton (2003).
[d] # relationships obtained by totaling numbers from tables in Appendix B for each category.
[e] Number of publications from the relevant list that were sources for the relationships.
[f] Some questions are used with more than one medium, thus, the total differs from the total in Table 2.1.

Sixty-six percent of the relationships considered metabolites in urine measurements (Table 2.2). The majority of these relationships were with DAP-based metabolites. Dust measurements have the next largest number of relationships with 31%. Both urine and dust have been shown in other studies, mostly with adults, to be more useful indicators of exposure level, and easier to collect from participants than other media. Few studies extended measurement collection to other media. Studies with measurements of other environmental media in conjunction with children's urine are not plentiful and were not evaluated.

The questions identified in the publications were reviewed for their ability to differentiate children's pesticide exposure levels based on whether the majority of the question's relationships were found to be statistically significant ($p \leq 0.05$) or marginally significant ($0.05 < p \leq 0.10$). This criterion summarizes the results of the relationships at a very high level, and does not take into account any differences in populations sampled or in interview/measurement situations for the studies described in the publications. Thus, the relationships for a question or category of interest should be reviewed in more detail with information in Section 4 and in Appendices B, C and D to determine their applicability to a particular situation.

Summary statistics for the exposure measurements, when available, were extracted from the publications for each relationship to provide researchers with additional information to help understand the relationships analyzed. When judging the appropriateness of a question for a future study, the researcher should also consider the difference between statistical and practical significance. The p-value associated with each relationship analyzed measures the strength of the relationship from the statistical perspective. Measures of central tendency, e.g., means, medians and coefficients from a multiple or logistic regression, give insights into the strength of the relationship from a practical level. The difference in the medians of two groups may be statistically significant, but both median values may be lower than measurement levels of interest for mitigating potential exposure. Thus, the magnitude of the difference between the two groups may not be useful for practical considerations.

Dust and urine measurements were found in 97% of the relationships. Measurements for the other media were found in only two of the 20 publications: Sexton (2003) and Simcox (1995). The relationships for each question and chemical/metabolite combination were reviewed to determine the question's effectiveness in differentiating the exposure levels. Not all question/chemical combinations were evaluated in the studies to the same extent. The number of relationships in which a question is evaluated, especially when the question is used with more than one study population, gives additional credence to the question as a potential differentiator. Generally the questions showing the most effectiveness are:

- residential pesticide use (inside and outside)
- occupation of household members
- child's characteristics (age, ethnicity, income)
- family hygiene practices
- household dust.

Several other questions also show some effectiveness:

- pets
- household location (urban vs non-urban)
- dietary behaviors (organic food)
- exposure levels of household members
- health status (diseases)
- smoking behaviors
- proximity to agricultural fields (for house dust only).

The number of relationships evaluated for the second group of questions was small, indicating that their effectiveness has not been tested as extensively as for the questions in the first group.

For urine measurements, questions showing usefulness as indicators of a child's pesticide exposure level cover the areas of residential pesticide use both indoors and outdoors, household occupation, subject's personal characteristics, family hygiene practices, and smoking behavior. Each of these indicators seems plausible, in that such relationships have been seen in previous investigations of environmental exposures (e.g., lead exposure in children). Some smoking activities were identified as potential differentiators (section 4.2.5.5); however, considerations regarding the study population in which they occurred and the very limited transferability of any pesticides through second-hand smoke makes this question less effective for purposes of this project. For dust measurements, the questions showing usefulness as indicators of a child's pesticide exposure level cover the areas of household occupation, residential proximity to spraying, and family hygienic behavior. Each of these indicators also seems plausible in terms of pesticides being present in the child's environment. These questions represent potential exposure from the take-home pathway and from agricultural pesticide spraying. A list of the specific questions and chemical/metabolite combinations found to be generally effective as differentiators of the exposure levels are presented in section 2.5.

The set of question categories used in this report provides one perspective for organizing the relationships. Three risk or exposure factors related to the take-home or para-occupational exposure pathway were analyzed as separate categories in this report: household occupation, family hygiene practices, and work exposure/practices. Household occupation was considered a source that would result in measurable differences in children's pesticide exposures, because it may represent a surrogate for the actual exposure levels of household members employed in agriculture. Children may be exposed to agricultural chemicals through this pathway and their exposure levels are dependent on the occupational status, work, handling, and hygiene practices of agricultural workers in their households.

Two other risk factors examined in this report also contribute to the para-occupational exposure pathway. Family hygiene practices and work exposure/practices were considered behavioral practices that could modify pesticide exposure to agricultural workers and their family members. There were fewer relationships in these two categories because the studies under review were primarily environmental exposures studies conducted in agricultural communities with a focus on children. If these studies had been strictly occupational exposure assessment studies, more questions related to the work and family hygiene practices might have been included in these studies.

2.3.2 Children's Pesticide Exposure Study (Yuma Study)

A study of children's exposure to pesticides was conducted in Yuma, Arizona for 152 households. In cooperation with eight local schools in the study area, families who were permanent residents of the area with children in kindergarten or first grade were self-selected to participate in a study conducted from October 1999 through February 2000. A urine sample was collected from each of these children (principal participants) and from any sibling in the household between the ages of 2 and 11 years. The urine samples were measured for the six most common dialkylphosphate (DAP) metabolites associated with OP pesticides. A dust sample was collected from each household, and from classrooms, with principal participants. These samples were measured for specific organophosphorous (OP), organochlorine, pyrethroid, and carbamate pesticides. A questionnaire regarding characteristics and practices of the family and the principal participant child was administered to each household. The study included 152 children as principal participants and 127 siblings. A total of 244 urine samples were available for analysis. Dust samples were available from 152 households and from 25 kindergarten and first-grade classrooms in six of the participating schools.

In the Yuma Study report (CDC 2002), the urine, dust, and questionnaire data were analyzed in order to describe levels of pesticide exposure and to identify any associations between questionnaire data and pesticide exposure levels. Traditional statistical techniques were performed to test predefined hypotheses. Urine measurements from all children in a household, household and school dust measurements, and responses for a selected subset of questions were included in the statistical analyses.

A second set of statistical analyses was performed on the Yuma study data specifically for this project. The analyses included only principal participants from the eight schools and two grades in the initial study design. A data mining approach was used to identify potential predictors without specifying a priori hypotheses between the biomarker measurements and the questions and dust measurements, that is, the approach was used to explore the relationships that exist in the data (Hand 1999).

The statistical analyses in CDC (2002) focused on six DAPs (DEP, DETP, DEDTP, DMP, DMTP, DMDTP) and the molar-weighted sums of the ethylated and methylated DAPs (Appendix F).

Table 2.3 Questions and Dust Measurements from the Yuma Study Having Strong Relationships with the DAPs, Adjusted for Creatinine (CDC 2002)

	DEP, DETP, or DEDTP[a]	DEAP[b]	DMP, DMTP, or DMDTP[a]	DMAP[c]
Questions[d,e]				
Used pesticide inside home in last month	X	X	X	
Distance from home to agricultural field	X			
Father working in agriculture			X	
Other adult in house working in agriculture	X	X	X	
Father, mother or other adult working in agriculture			X	
Household and/or School Dust[f]				
carbaryl		X		X
chlorpyrifos[g]	X[g]	X[g]	X	X
cis-permethrin	X	X	X	X
cy-permethrin	X	X	X	X
diazinon[g]	X[g]		X	X
gamma-chlordane		X		
proxopur	X	X	X	
trans-permethrin	X	X	X	X

[a] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.

[b] DEAP is a summary variable made from summing molar weights of DEP, DETP and DEDTP, and is noted as DEOP in CDC (2002). (Concentrations < Limit of detection (LOD) were replaced with LOD/2.)
[c] DMAP is a summary variable made from summing molar weights of DMP, DMTP and DMDTP, and is noted as DMOP in CDC (2002). (Concentrations < LOD were replaced with LOD/2.)
[d] See Tables 4.3.4, 4.3.5, and 4.3.6 for relationships with specific metabolites or sums.
[e] Full description of questions can be found in Table 3.1.
[f] See Tables 4.3.7, 4.3.8, 4.3.9, and 4.3.10 for relationships with specific metabolites or sums
[g] These are the only OPs for which relationships with ethylated DAPs are expected. All other significant relationships may be indicative of heavy pesticide use, although they do not correspond to the metabolite found.

Of the questions analyzed, recent indoor pesticide use, household members working in agriculture, and distance from home to agricultural fields have statistically significant relationships with the ethylated DAP sum, and individual ethyl and methyl DAPs (Table 2.3). The directions for some of the relationships, however, are the opposite of what might be expected based on current knowledge, that is, an exposure activity is not related to a higher measurement level. Dust measurements of chlorpyrifos and the permethrins are strongly related with both the ethylated and methylated DAP sums. Some of the significant relationships between house/school dust measurements and the DAP measurements are unexpected. These may be indicators of heavy pesticide use, although they do not correspond to the metabolite found. The regression coefficients for these statistical analyses are very small and may indicate that the relationships are not necessarily practically significant. The report authors note:

> The regression models in which the slopes were small but were statistically significant may suggest either that a) true associations existed, but the numbers of significance were less than the numbers measured in the statistical programs or b) the associations were meaningless and based solely [on] the probability of finding statistical significance if enough tests were run. (CDC 2002)

Another set of analyses was conducted for this project using the data mining technique Classification and Regression Trees (CART). Six scenarios (Table 2.4) of potential predictors containing questions, and house and school dust measurements were evaluated for the sums of ethylated and methylated DAPs (Appendix F). The scenarios covered three levels of increasing measurement burden (questions, household dust, and school dust) with two sets of questions for each level.

Table 2.4 Questions and Measurements Included in the Yuma Study CART Analysis Scenarios for Each DAP Sum

Scenario	Full Set of Questions[a]	Limited Set of Questions[b]	House Dust Measurements	School Dust Measurements
1	X			
2		X		
3	X		X	
4		X	X	
5	X		X	X

Scenario	Full Set of Questions[a]	Limited Set of Questions[b]	House Dust Measurements	School Dust Measurements
6		X	X	X

[a] Full set includes limited set of questions.
[b] Questions from full set considered more likely to be predictors of children's pesticide exposure level.

Only the limited set of questions was included in all six scenarios. Thus, the remaining questions and dust measurements did not have as many opportunities to be selected as predictors in the CART analyses. The criterion used to determine whether a question or dust measurement had a strong relationship with one of the DAP sums was that it was selected in the CART analyses a majority of times (> 50%) based on the number of scenarios in which the predictor was included. Thus, for a house dust measurement to denote a strong relationship with the biomarker measurement, the dust measurement would have to be selected in at least three of the four CART analyses. This type of criterion identifies predictors that are strong, because they are more universal across the scenarios.

The CART analyses were conducted using responses from the principal participant children in the initial study design, that is, the children who were in one of the eight schools and were in kindergarten or first grade. All six scenarios were conducted with 130 principal participants. An explanation of the CART technique and details of the CART analyses can be found in Appendix G.

Table 2.5 Questions and Dust Measurements from the Yuma Study Having Strong Relationships with the Sum of Methylated DAPs Based on the Data Mining Approach

Predictor	Description	LTD Q[a]	% Scenarios Predictor Selected	Number of Scenarios with Predictor Included
Questions				
HEIGHT	Child's height (inches)	X	100	6
NCATWRKD	Father's occupation -- categories		67	3
SCHOOL	Child's school	X	83	6
WEIGHT	Child's weight (lbs)	X	67	6
WHEEL	Distance between home and field - rotary wheel		67	3
WHERTIME	Room where child spends most awake time	X	100	6
WHNCHEMO	Last time field treated with pesticides?		100	3
House Dust Measurement Sums[b]				
WCHLPYRF	Weighted chlorpyrifos		100	4
WDIAZNON	Weighted diazinon		75	4
WPERMSUM[c]	Weighted sum of cis-permethrin and trans-permethrin		100	4

School Dust Measurement Sums[b]				
None				

[a] X -- Question was in the limited subset and thus included in all six scenarios.
[b] Description of measurement sums can be found in Appendix F.
[c] Although these relationships do not correspond to the metabolite found, they may be indicative of heavy pesticide use or may be a surrogate for some other exposure event.

Questions related to agricultural fields and child size, and household dust measurements were selected as having strong relationships for the sum of methylated DAPs; however, school dust measurements were not selected (Table 2.5). Initial analyses for the sum of ethylated DAPs included CHLDTM3 (Child spends time at school) as a strong predictor, however, it was difficult to understand the responses in the context of the population analyzed, that is, children in kindergarten and first grade. Analyses were then performed excluding CHLDTM3. Subsequently, CHLDTM3 was considered a possible indicator of additional time spent at school, which might reflect additional exposure from the home environment for the "NO" respondents because they were not spending more time at school (Table G.3.6). Questions relating to diet, residential pesticide use, time spent at home, and agricultural fields, and measurements from both the house and school were selected for the sum of the ethylated DAPs excluding CHLDTM3 (Table 2.6).

Table 2.6 Questions and Dust Measurements from the Yuma Study Having Strong Relationships with the Sum of Ethylated DAPs Based on the Data Mining Approach (Excluding CHLDTM3)

Predictor	Description	LTD Q[a]	% Scenarios with Predictor Selected	Number of Scenarios with Predictor Included
Questions				
ETHNIC	Child's ethnic and racial background		67	3
HOURAWAY	Number hours/wk child not at home	X	100	6
NRMSPRYD	Number of rooms sprayed last month		100	3
VEGGIES	How often child eats local fresh fruit/veg?		67	3
WEIGHT	Child's weight (lbs)	X	100	6
WHEEL	Distance between home and field - rotary wheel		100	3
WHNCHEMO	Last time field treated with pesticides?		100	3
House Dust Measurement Sums[b]				
WCHLPYRF[c]	Weighted chlorpyrifos		75	4
WDUSTBAL	Weighted sum of dust analytes except OP pesticides		100	4
WDUSTSUM	Weighted sum of all dust analytes		100	4
WPERMSUM	Weighted sum of cis-permethrin and trans-permethrin		100	4
School Dust Measurement Sums[b]				

Predictor	Description	LTD Q[a]	% Scenarios with Predictor Selected	Number of Scenarios with Predictor Included
SWCHLPYR[c]	Weighted chlorpyrifos		100	2
SWOPBAL	Weighted sum of OP pesticides except chlorpyrifos, diazinon, permethrins, and o-phenylphenol		100	2
SWOPSUM	Weighted sum of OP pesticides		100	2

[a] X -- Question was in the limited subset and thus included in all six scenarios.
[b] Description of measurement sums can be found in Appendix F.
[c] Although these relationships do not correspond to the metabolite found, they may be indicative of heavy pesticide use or may be a surrogate for some other exposure event.

2.4 Summary of Results from Two Approaches

The Yuma Study report (CDC 2002) looked at each question or measurement individually and included siblings as well as principal participants using a general linear estimating model with repeated measures for 152 households. The potential risk or exposure factors selected for analysis were the subset of the full set of questions that were available for siblings as well as principal participants, that is, the child's physical characteristics and household characteristics or practices. The data mining approach used all the questions and measurements simultaneously in CART analyses for only 130 principal participants in kindergarten and first grade. Given these and other differences, it may be useful, with caution, to look at a summary of the predictors selected under both approaches to evaluate the universal strength of the predictors. It should be noted that some of the significant relationships between house/school dust measurements and the DAP measurements may be indicators of heavy pesticide use, although they do not correspond to the metabolite found.

Table 2.7 Comparison of Selected Predictors from Yuma Study Report[a] (CDC 2002) and Data Mining Approach[b] for Methylated Sum of DAPs[c]

Yuma Study Report	Data Mining Approach
No Questions	Child's characteristics (height, weight)
	Proximity to agricultural fields, spraying conditions
	Father's occupation
	Where in house child spends time[d]
	Child's school[d]
Household dust[e]: diazinon, chlorpyrifos, permethrins, carbaryl	Household dust[e]: diazinon, chlorpyrifos, permethrins
School dust[e]: diazinon, permethrins,	School dust: none

[a] Based on Tables 4.3.4, 4.3.7, and 4.3.9 and the molar-weighted sum of methylated DAPs (adjusted for creatinine).
[b] Based on Table G.3.5 and log (molar-weighted sum of methylated DAPs-adjusted for creatinine).
[c] See definition in Appendix F.

[d] Questions were not analyzed in CDC (2002) because responses were not available for siblings.
[e] Although these relationships do not correspond to the metabolite found, they may be indicative of heavy pesticide use or may be a surrogate for some other exposure event.

Table 2.8 Comparison of Selected Predictors from Yuma Study Report[a] (CDC 2002) and Data Mining Approach[b] for Ethylated Sum of DAPs[c]

Yuma Study Report	Data Mining Approach
Recent use of pesticides inside home	Recent use of pesticides inside home
	Child's characteristics (weight, ethnicity)
Other adult in household working in agriculture	
	Proximity to agricultural fields, spraying conditions
	Child's time spent away from home[d]
	Diet - local fruits/vegetables[d]
Household dust[e]: OPs, permethrins, non-OPs	Household dust[e]: OPs, permethrins, non-OPs
School dust[e]: permethrins	School dust[e]: OPs

[a] Based on Tables 4.3.4, 4.3.7, and 4.3.9 and the molar-weighted sum of ethylated DAPs (adjusted for creatinine).
[b] Based on Table G.3.4 without CHLDTM3 as a potential predictor and log (molar-weighted sum of ethylated DAPs-adjusted for creatinine).
[c] See definition in Appendix F.
[d] Questions were not analyzed in CDC (2002) because responses were not available for siblings.
[e] Although these relationships do not correspond to the metabolite found, they may be indicative of heavy pesticide use or may be a surrogate for some other exposure event.

The analyses in the Yuma Study report (CDC 2002) consider questions and measurements that would apply as risk factors to the siblings as well as the principal participants, and for which there were available responses. These factors may affect explanations of the variability of the pesticide metabolite levels across siblings within a household. The data mining approach focuses the analyses on a group of children with less diverse characteristics in terms of school and grade level and includes all questions regarding the principal participants. For the sum of methylated DAPs, no pesticides in household dust were similar across both approaches and no questions were found significant in the Yuma Study report (Table 2.7). For the sum of ethylated DAPs, recent use of pesticides inside the home, and OPs, non-OPs, and permethrins in the household dust stand out as differentiators of children's pesticide exposure level across both approaches (Table 2.8). The difference in analysis techniques and the difference in participants included in the analyses may help explain the differences in the predictors selected across the two approaches. Also, some questions regarding sibling activities were not analyzed in CDC (2002) because that information was not collected as part of the study design. The best use of these results is as "indicators" of predictors that are more useful in differentiating the exposure levels.

Two approaches were taken in this project to identify questions that were useful in differentiating children's pesticide exposure levels as a screening tool for selecting participants of interest in future exposure studies. One approach reviewed relationships with questions described in the literature from previous exposure studies. The second approach reviewed relationships with questions based on a study of children's pesticide exposure in Yuma, Arizona.

Table 2.9 Summary of Predictors Selected as Useful in Differentiating Children's Pesticide Exposure Levels Across Two Approaches

Literature Review[a]	Yuma Study[b]
Residential pesticide use	Residential pesticide use
Pets[c]	
Occupation of household members	Occupation of household members
Household location: urban vs non-urban[c]	
Child's personal characteristics	Child's personal characteristics
Dietary behaviors (organic food)[c]	Dietary behaviors (local fruits/vegetables)
Family hygiene practices	
Exposure levels of household members[c]	
Health status (diseases)[c]	
(Proximity to agricultural fields)[d]	Proximity to agricultural fields, spraying conditions
	Where child spent time at home/not, or within home

[a] Based on the "c" tables: Tables 4.2.6.c - 4.2.21.c.
[b] Based on Tables G.3.5 and G.3.7.
[c] Only a small number of relationships evaluated these questions.
[d] Proximity to agricultural fields for the literature review was related to dust measurements only.

The types of questions that seem to be strong differentiators of children's pesticide exposure levels based on both approaches are:

- occupation of adults living in household
- residential pesticide use
- residential proximity to spraying and agricultural fields
- characteristics of the subject that may indicate potential exposure activities
- family hygiene practices that may mitigate the take-home pathway exposure
- where the child spends time (in home, away from home)
- diet with respect to locally-grown fresh fruits and vegetables (Table 2.9).

It seems clear from this review that children's proximity to pesticide use can increase the likelihood of their exposures, whether the source is residential pesticide use, agricultural pesticide use near the residence, or pesticide exposure in the workplace that results in residential contamination. It is also evident from one study that replacement of conventionally produced fresh fruits and vegetables (i.e., pesticides used in production) with organic produce can result in substantial decreases in urinary pesticide metabolite levels.

Future studies that use biological monitoring and questionnaires should draw upon recent research to refine study protocols. Several suggestions are provided in the following section of recommendations.

2.5 Recommendations

2.5.1 Effective Differentiators of Exposure Level

Based on an evaluation of the relationships found in the literature review, forty-two questions were identified as effective in differentiating exposure levels of at least one chemical/metabolite in Table 2.11. These questions are offered as a resource of recommended questions with specific chemicals or metabolites for future study designs. Note that the questions were evaluated here as a screening tool to create an enriched population of participants with higher exposure levels. Thus their future use is better suited to similar purposes.

The chemicals and metabolites found in the publications were assigned to seven groups, for presentation purposes, based on medium and type of chemical metabolite measured (Table 2.10).

Table 2.10 Description of Code Names and Groups Assigned to the Chemicals and Metabolites, Sorted by Code

	Chemicals/Metabolites		
Medium	**Grouping**	**Code**	**Description**
urine	1-Non-DAP	1NAP	1-Naphthol
urine	1-Non-DAP	4NITR	4-Nitrophenol
other[a]	6-Chemical	ATZ	Atrazine
urine	1-Non-DAP	ATZM	Atrazine mercapturate
other	6-Chemical	AZM	Azinphosmethyl
other	6-Chemical	AZMPH	Azinphosmethyl+Phosmet
other	6-Chemical	CHLR	Chlorpyrifos
urine	3-DAP Sum	DAP1	DMP+DMTP+DMDTP+DEP+DETP+DEDTP
urine	4-DAP Detect	DAP2	DEP, DETP, DEDTP, DMP, DMTP (at least one detectable measurement)
urine	5-DAP High	DAP3	DEP, DETP, DEDTP, DMP, DMTP (at least one high measurement)[b]
urine	2-DAP	DEDTP	Diethyldithiophosphate (DEDTP)
urine	2-DAP	DEP	Diethylphosphate (DEP)
urine	2-DAP	DETP	Diethylthiophosphate (DETP)
urine	2-DAP	DMDTP	Dimethyldithiophosphate (DMDTP)
urine	2-DAP	DMP	Dimethylphosphate (DMP)
urine	2-DAP	DMTP	Dimethylthiophosphate (DMTP)
other	6-Chemical	EPAR	Ethyl parathion

	Chemicals/Metabolites		
Medium	**Grouping**	**Code**	**Description**
urine	3-DAP Sum	ETHL1	DEP+DETP
urine	3-DAP Sum	ETHL2	DEP+DETP+DEDTP
urine	4-DAP Detect	ETHL3	DEP, DETP, DEDTP (at least one detectable measurement)
other	6-Chemical	MAL	Malathion
urine	1-Non-DAP	MDA	Malathion dicarboxylic acid
urine	3-DAP Sum	MTHL1	DMTP+DMDTP
urine	3-DAP Sum	MTHL2	DMP+DMTP+DMDTP
urine	4-DAP Detect	MTHL3	DMTP (detectable measurement)
urine	4-DAP Detect	MTHL4	DMP, DMTP (at least one detectable measurement)
urine	5-DAP High	MTHL5	DMP, DMTP (at least one high measurement)[b]
urine	7-Metabolite NA	NA	Specific metabolite was not provided
other	6-Chemical	OPSUM	OP sum[c]
other	6-Chemical	PHSM	Phosmet
urine	1-Non-DAP	TCPY	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled).
[b] See definition of high measurement in Azaroff (1999)
[c] OP sum = azinphosmethyl, chlorpyrifos, malathion, and phosmet.

Forty-eight questions across 12 question categories were considered effective differentiators of the exposure measurement levels of at least one chemical/metabolite evaluated in the relevant publications (Table 2.11). Their effectiveness was determined by whether a majority (> 50%) of the relationships for a given chemical/metabolite were statistically or marginally significant.

Table 2.11 Questions Considered Effective Differentiators of Children's Pesticide Exposure Levels Based on a Literature Review of Previous Exposure Studies

Medium	Q Category	Q #[a]	Q Description[b]	Chemicals/ Metabolites [c]
Dust				
	Residential pesticide use	Q119	Outside Treated[d]	CHLR
	Household characteristics	Q202	Property Used As a Farm[d]	CHLR
		Q213	Size of Household	AZM
	Residential sources (environmental measures)	Q303	Outdoor Soil	EPAR
	Household occupation	Q401	Agricultural Workers in Household	AZM

Medium	Q Category	Q #[a]	Q Description[b]	Chemicals/ Metabolites [c]
		Q404	Applicator vs Farmworker	AZMPH, EPAR
		Q405	Applicator vs Non-applicator	CHLR, EPAR
		Q407	Applicator and Farm worker vs Reference	AZM, AZMPH, CHLR, EPAR, PHSM
		Q412	Fieldworker vs Pesticide Handler	AZM
		Q415	Tree Thinning	OPSUM
		Q416	Number in Household with High Pesticide Contact	OPSUM
	Residential proximity to agricultural fields	Q501	Proximity of Home to Pesticide-Treated Farmland/Orchard	AZMPH, EPAR
	Residential location	Q605	Vehicle vs House	AZM
	Family hygiene practices	Q1006	Work Clothes Worn Indoors	AZM, OPSUM
		Q1009	Number of Weeks Since Last Vacuuming	OPSUM
Indoor Air				
	Household characteristics	Q202	Property Used As a Farm[d]	CHLR
Personal Air				
	Residential pesticide use	Q102	Inside Treated	CHLR
		Q124	Level of Pesticide Use[d]	ATZ
Soil				
	Household occupation	Q409	Farmer and Farm Worker vs Reference	AZM
Solid Food				
	Residential pesticide use	Q119	Outside Treated[d]	CHLR
Urine				
	Residential pesticide use	Q104	Inside Treated - Bedroom	TCPY
		Q106	Inside Treated - Closets	TCPY
		Q108	Inside Treated – Dining Room	TCPY
		Q111	Inside Treated -- Living Room	TCPY
		Q117	Inside Treated -- Other Room	TCPY
		Q119	Outside Treated[d]	MDA, TCPY
		Q120	Garden Treated	TCPY, ETHYL1, METHYL2
		Q121	Lawn/Yard Treated[d]	TCPY
		Q124	Level of Pesticide Use[d]	MDA, TCPY

Medium	Q Category	Q #[a]	Q Description[b]	Chemicals/ Metabolites [c]
		Q125	Frequency Personal Application Inside	TCPY
		Q126	Frequency Personal Application Outside	TCPY
		Q127	Inside/Outside Treated by Family Member	ETHYL3, METHYL3, METHYL4, DAP2, DAP3
		Q130	Personally Mixed Pesticide Inside	TCPY
	Household characteristics	Q208	Pets in House	METHYL2
		Q209	Pets Inside/Outside House[d]	MDA
		Q211	Existence of Garden or Vegetable Garden[d]	ETHYL1, MDA
	Residential sources (environmental measures)	Q301	Household Dust	METHYL2, NA
	Household occupation	Q402	Household Member Spraying Fields	DAP2, DAP3, ETHYL3, METHYL3, METHYL4, METHYL5
		Q403	Recent Fieldwork	DAP2, DAP3, METHYL4, METHYL5
		Q406	Applicator vs Reference	DMTP
		Q407	Applicator and Farm Worker vs Reference	DMTP, METHYL1
	Residential proximity to agricultural fields	Q501	Proximity of Home to Pesticide-Treated Farmland/Orchard	DMTP
	Residential location	Q601	Urban vs Non-urban	TCPY
	Subject's personal characteristics	Q702	Age	DAP1, METHYL2
		Q703	Ethnicity	1NAP, MDA
		Q705	Income	1NAP, MDA, TCPY, DMTP, DAP1
	Child's behaviors	Q806	Loading from Hand Wipe	DAP1
	Dietary behaviors	Q904	Organic Diet	METHYL2
	Smoking-related activities	Q1101	Current Smoker[e]	TCPY
		Q1102	Subject Smoked[e]	TCPY
	Related exposure levels	Q1302	High Levels in Adult Household Members	DAP2, DAP3, METHYL4
	Health	Q1403	Bowel Disease	TCPY
		Q1405	Intestinal Disease	TCPY
		Q1406	Ulcers	TCPY

[a] For some of the significant relationships, the effect of the exposure factor was not in the direction expected.

See Appendix C for details on specific relationships.
[b] See Appendix C for specific question phrasings included under each question description.
[c] Chemicals or metabolites for which > 50% of the relationships with the question were statistically or marginally significant. See Table 2.10 for chemical/metabolite description.
[d] See section 4.2.2 regarding relationships from Sexton (2003).
[e] Included only in Krinsley (1998) (section 4.2.5.5).

2.5.2 Urinary Metabolite Monitoring

A substantial proportion of the analysis in this report has focused on the association between questionnaire data and pesticide metabolites in children's urine. These analyses have been conducted on the assumption that the urinary metabolite measurements provide an accurate estimate of children's exposure; that is, if statistical associations were not observed, it was concluded that the questionnaire information was probably not a useful indicator of children's pesticide exposure. Yet we know that the metabolites under study are processed and excreted relatively quickly in humans (1-3 days) and, therefore, represent recent exposures. In contrast, most of the questions asked of parents or children were of a general nature in terms of the time frame of a particular activity or behavior. It is, therefore, worthwhile to consider the variability in measurements in urinary pesticide metabolites.

Nearly all of the studies examined in this report have used spot urine samples as the outcome that is compared to questionnaire data. A number of these studies have collected at least two spot samples from children, but only one collected complete urine samples over a fixed time period (Curl 2003). Several recent exposure studies have observed that intra-individual variability in pesticide metabolite concentrations in urine can be high (Macintosh 1999, Adgate 2001, Koch 2002). In these studies, an attempt was made to address this issue by collecting samples on a repeated basis: Macintosh (1999) collected up to six samples from each of up to 80 adult participants in the Maryland NHEXAS study, but the samples were approximately eight weeks apart; Koch (2002) collected samples from pre-school children on a bi-weekly basis for approximately one year. In both of these studies, the urine samples were essentially independent from one another in relation to exposure sources, although in the Koch study the 4-6 week agricultural spray season was identified as a time of elevated exposure. Adgate (2001) introduced more of a TEAM (Total Exposure Assessment and Monitoring) study design, that is, multiple samples over time, by collecting three morning voids from children in the course of one week. Such repeated measures would have a better chance of separating high and low exposed children if, for instance, a pesticide application had occurred at the residence at the beginning of the week. However, none of these study designs addresses directly the high day-to-day variability that seems to be the norm for pesticide metabolite excretion in children, even when creatinine adjustments are performed. In contrast Curl (2003) collected a full 24-hour urine sample to compare conventional and organic dietary behavior, and was able to demonstrate a large difference in exposure between these two groups. Krieger (2001) also collected 24-hour urine samples from children after the use of total aerosol release devices (foggers) in residences and was able to discern clear patterns in child exposure levels over time.

Two occupational exposure studies may serve as useful models for the design of future studies of children's pesticide exposure that involve urinary metabolite monitoring. Arbuckle (2002) examined the relationship between self-reported behaviors during pesticide applications and urinary excretion of two herbicides--2,4-dichlorophenoxyacetic acid (2,4-D) and 4-chloro-2-methylphenoxyacetic acid (MCPA). Urine samples were complete 24 hour voids from the beginning of application through the following day. With this sampling scheme the questionnaire's prediction of exposure had a sensitivity of 57% and a specificity of 86% for 2,4-D; for MCPA the sensitivity and specificity were 92% and 67%, respectively. A multivariate analysis was able to identify several variables as predictive of urinary metabolite concentrations. Harris (2002) studied commercial pesticide applicator exposure collecting two consecutive 24-hour urine samples from each participant. Investigators then modeled weekly exposure and dose based on knowledge of the amount of pesticide used by each applicator. This analysis was able to identify two major exposure factors: type of nozzle used and use of gloves during application. These studies suggest that if complete 24 or 48 hour urine samples are collected, it may be possible to identify major risk factors for exposure.

2.5.3 Questionnaire Validation

Few of the studies analyzed in this report have used validated questionnaires as a part of their examination of children's pesticide exposure. Questionnaire validation includes a test for accuracy (i.e., determine if the answer reported on the questionnaire by the study participant is correct), usually by comparison of the study instrument results with a "gold standard" for some subset of the study population. For example, answers to a question regarding a child's absence from school could be checked against school attendance records. Validation may also include tests for reliability (i.e., determine if the study participant provides the same answer to the question when tested on several occasions.) Validity of questionnaire data is an essential consideration in epidemiologic studies and future studies of children's pesticide exposure should be preceded by validation studies. A good example of this approach is available from the ongoing Agricultural Health Study conducted by the National Cancer Institute in collaboration with other federal agencies in the United States (Alavanja 1994). Dosemeci (2002) developed a quantitative metric for applicator exposure based on an analysis of the existing scientific literature. This metric provides quantitative adjustment factors for certain behaviors (e.g., use of gloves) reported in questionnaires and provides the basis for classifying each applicator's exposure for epidemiologic analysis. A critical component of the development of this model has been its validation through biological monitoring. The U.S. Environmental Protection Agency has conducted a study of pesticide applicators, collecting urinary metabolite data and comparing these to the questionnaire data collected by the National Cancer Institute (Thomas 2004). This work has demonstrated good correlations between self-reported behavioral data from applicators and the urinary metabolite data. It would behoove those involved in the study of children's pesticide exposure to consider this approach in the development of epidemiologic investigations.

2.5.4 Objective Measures of Children's Behaviors

Studies of children's pesticide exposure should work to improve the quality of data related to behavior. At present, researchers rely primarily on parental reports of behavior for young children. Yet the validity of parental reports has not been scrutinized in a systematic fashion. Duplicate diet sampling over 24 hours (Macintosh 1999, Fenske 2002) is a good example of an objective measure of pesticide exposure for the dietary pathway. In a recent study, researchers have found that NHEXAS-style parental diaries of children's time-location (macro-activities) were not accurate when compared with global positioning system (GPS) measurements over a 24 hour period (Elgethun 2003, Elgethun 2004, Elgethun 2005). Similarly, parental reports of children's contact with objects and mouthing behavior (micro-activities) are not necessarily accurate when compared to videotaping (Reed 1999, Black 2005). There is clearly a need for more objective measures of children's activities and behaviors in conjunction with systematic biological monitoring to ensure identification of key predictors of children's exposure to pesticides.

3.0 METHODOLOGY

3.1 General Description of Approach

Reconciling the sources and outcomes of exposure is a complex process because of the multitude of potential sources, interactions between sources and other factors, and timing issues between an actual exposure and evidence of the exposure. When preparing for an exposure study, investigators are likely to take into consideration both the hypothetical and observed relationships described in the research literature for their study design. Examples of hypothetical or theoretical relationships are found in the general environmental health paradigm (Sexton 1995a) as models for source, concentration, exposure, and dose. Examples of observed relationships are those identified in data analyses from an exposure study as in Clayton (1999) which described the result of examining question-measurement relationships for the NHEXAS Region 5 Study.

As a reference for the design efforts of the Pesticides in Young Children Border States Program, and for other future exposure studies, this project compiled the observed relationships between questions and measures of children's exposure to pesticides. The assimilation and review of these relationships was performed using two approaches:

- A literature review of previous exposure studies to summarize the existence of such quantitative and qualitative relationships, and
- An analysis of a recent children's pesticide exposure study in Yuma, Arizona, which included questionnaires and measurements.

Relationship, as used in this report, is defined as a systematic correspondence between the values of two variables from an exposure study, that is, questionnaire responses and analytical measurements. This correspondence may or may not be statistically significant. Similarities and differences in the results from the two approaches are discussed in section 4 (Results and Discussion).

3.2 Literature Review Methods

3.2.1 Sources

The literature review began with a search of several online citation indexes available at the University of Nevada, Las Vegas library using keywords pertinent to this project's objective. The following indexes were searched: MEDLINE (PubMed), Medline (FirstSearch), Infotrieve, NTIS (National Technical Information Service), Wiley Interscience Journals, Environmental Sciences And Pollution Management, and Toxline. The keywords survey, questionnaire, children, pesticide, measurement, and biomonitoring were used in combination to search the indexes. When an index limited the number of keywords used, multiple searches were performed using subsets of the keyword list.

Abstracts of over 100 citations from the search results were evaluated to determine if they fit the project's focus. To be considered for the next level of review, a publication was required to:

- address the pesticide exposure of children,
- have collected monitoring samples, preferably urine, and
- indicate the use of a survey or questionnaire in the study.

Two types of publications were excluded from further review: those describing studies of infants or pre-natal situations and those that did not include an evaluation of relationships between questions and monitoring measurements. The former type of publication was not included because the exposure scenarios for children at such very young ages are somewhat different from those for children of toddler age and up. Including such publications in this review might add another layer of variability in evaluating the literature results.

Other sources of publications or pertinent results were also considered. They included:

- references cited in the relevant articles from the first round of searches,
- Masters' theses that were the basis for some of the relevant articles,
- Status Report on Biological Monitoring Research Relevant to Aggregate Exposure Assessment under the Food Quality Protection Act (Fenske 1998), and
- Report on the Phase II NAFTA studies (USEPA 2002).

A more in-depth review of the publications considered potentially pertinent was performed with an adjusted set of criteria. To be included in the next round, a publication was required to:

- study pesticide exposure,
- describe relationships between questions and measurements from monitoring samples, and
- include children as part of the population studied.

These criteria expanded the base of articles with studies of children and adults for potential take-home exposure, while narrowing the list of pertinent articles to those that evaluated relationships. No limitation was placed on the pesticides considered; however, most of the relevant articles described organophosphorous (OP) pesticides because they are generally the most toxic of the pesticides. Although the primary interest was in biomarker data, relationships for any medium were noted.

Based on the second level of review, the publications were sorted into two groups: relevant and not applicable. The relevant publications were the basis for identifying the relationships to be reviewed (Table A.1). The rest of the publications were considered not applicable to this project's objective (Table A.2).

3.2.2 A Database of Relationships

A simple database was created using MS Excel to track the relationships noted in the set of relevant publications and to facilitate presentation of the relationships as tables for this report. For each relationship in the database, the following information was recorded:

- citation abbreviation,
- question,
- medium of the measurement,
- chemical or metabolite measured,
- type of statistical analysis performed to evaluate the relationship,
- statistical significance of the analysis,
- p-value for the statistical analysis (as available),
- study sub-population included in the analysis,
- groups compared in the analysis (depending on the type of analysis performed),
- descriptive statistics or parameters produced by the analysis (as available),
- descriptors for the chemical measurements, such as log transformed, adjusted for creatinine, etc., and
- comments.

An attempt was made to extract the maximum amount of information from each publication for the database. Any of the very few instances of interpretation or assumptions are noted in Appendix D.

To evaluate the track record of potentially effective questions for future studies, this report includes relationships that are both statistically significant and non-significant. Several publications listed or alluded to questions that were asked in the study interviews, but their relationships with a measurement were not addressed in the publication. Phone or email contact was made with the respective principal author to determine the status of the missing relationship descriptions while recognizing the boundaries of unpublished research. In most cases, it was determined that the relationships were excluded by the authors because the relationships were not significant, were never analyzed, were analyzed and reported in another article, or were to be reported in future publications. Information about these unaddressed relationships was not included in the database.

Lastly, to facilitate the presentation of the literature review, several levels of organization were added to the database. The questions were first grouped into 14 categories, such as residential pesticide use, dietary habits, and household occupation. These categories were then grouped into three super categories of risk factors: source, behavior, and other. An abbreviated version of the question was assigned to each relationship to allow questions with similar intent, but slightly different phrasing, to be presented together.

The relationships extracted from the relevant publications are presented in Appendices B, C, and D. An evaluation of the questions' usefulness in differentiating levels of pesticide exposure in children is presented in section 4.2 (Results and Discussion) and section 2 (Summary and Recommendations).

3.3 Children's Pesticide Exposure Study

A recent study of children's exposure to pesticides from Phase II of the Pesticide Exposure and Health Effects on Children Initiative (Section 1.6) was also considered. A report (CDC 2002) describing the study and its evaluation of predefined hypotheses was reviewed in a manner similar to the literature review. Data from the study were also made available for exploratory analysis to determine if relationships, other than those predefined by the study's objective, might surface.

3.3.1 Background

The U. S. Centers for Disease Control and Prevention (CDC), specifically the Health Studies Branch, and the Toxicology Branch of the National Center for Environmental Health, in collaboration with the U. S. Environmental Protection Agency (U.S. EPA), and the Arizona Department of Health Services, conducted a study of pesticide exposure in children living in Yuma County, Arizona. The Children's Pesticide Exposure Study is one of the studies funded by the Environmental Health Working Group in the Border 2012 Program (USEPA 2004b), through the Pesticide Exposure and Health Effects on Children Initiative, to assess the association of health outcomes in children with chronic exposure to pesticides. The study collected objective measures of pesticide exposure in the children to help determine the need for mitigation and prevention strategies for children and families living near the border. Its objective was to determine the impact of living, or attending school, near pesticide-treated fields on children's exposure to organophosphorous (OP) pesticides. Subsequently, this study will be referred to as the Yuma Study.

In cooperation with eight local schools in the study area, families who were permanent residents of the area with children in kindergarten or first grade were self-selected to participate in a study conducted from October 1999 through February 2000. Promatores, that is, lay health-care workers from a local non-government agency in Yuma, recruited a convenience sample of participants by sending informational flyers home with children in kindergarten and first grade, by approaching parents at Women, Infant and Children (WIC) clinics, and by referrals from other participants. The data collection was performed during a time period when large quantities of OP pesticides were expected to be applied to crops. The promatores performed the data collection including the administration of a questionnaire regarding characteristics and practices of the family and principal participant child. A urine sample was collected from each of these children (principal participants) and from any sibling in the household between the ages of 2 and 11 years. The urine samples were measured for the six most common dialkylphosphate (DAP) metabolites associated with OP pesticides. A dust sample was also collected from each household, and from classrooms, with principal participants. These samples were measured for specific OP, organochlorine, pyrethroid, and carbamate pesticides.

The study included 152 children as principal participants and 127 siblings. A total of 244 urine samples were available for analysis. Dust samples were available from 152 households and from 25 kindergarten and first-grade classrooms in six of the participating schools. The study analyzed the urine, dust, and questionnaire data to describe levels of pesticide exposure, and to identify any associations between questionnaire data and pesticide exposure levels.

The study report (CDC 2002) describes the statistical analysis approach that evaluated the predefined hypotheses between children's pesticide exposure and risk factors like distance from agricultural fields. Most of the analyses in this study were performed on urine measurements for the principal participant and the siblings in each household, included measures of intra-household correlation, and compared the measurements of principal participants with their siblings. Geometric means and 95% confidence intervals were calculated for variables that were not normally distributed. When considering the relationships between risk factors and measures of pesticide metabolites, regression models on log-transformed concentrations, controlling for intra-house correlation, were used. These relationships were evaluated for metabolite concentrations adjusted, and not adjusted, for creatinine. Regression models and Spearman correlations evaluated associations between the concentrations of the urinary metabolites, adjusted and unadjusted for creatinine, and household or school dust.

As a supplement to the initial findings in the Yuma Study report (CDC 2002), the study's data were also evaluated using a data mining approach. Data mining describes an analysis approach that searches through data for relationships that may or may not be defined a priori. This process is exploratory in nature in comparison to a confirmatory analysis that is interested in determining whether a proposed relationship adequately explains the observed set of data (Hand 1999). The data mining approach used in this project focused on identifying relationships that would be useful in classifying children by their OP pesticide exposure level, with a specific interest in being able to identify children with high or low exposure levels. The first stage of this approach prepared the data for analysis, the second stage reviewed basic relationships in the data, and the third stage performed classification type analyses. The data manipulation and analysis steps were carried out with SPSS versions 11.5 and 12.0 (SPSS, Inc., Chicago, IL), and S-Plus version 6 (Insightful, Inc., Seattle WA).

3.3.2 Stage 1 – Data Preparation

The Yuma Study data were reviewed to determine the types of analyses to be performed. Adjustments were made to the data only to facilitate analyses and not to change the intent of any responses. These adjustments included changes in data formats, the addition of code values to describe certain situations, the creation of additional variables based on the original data, and the identification of subgroups within the study to be used for the analyses. Steps were taken to assure the quality of any changes made to the data and for any additional variables created. A general description of the adjustments made to the Yuma Study data is described in Appendix G.

After making these adjustments, the questions from the study were reviewed to determine which would be used in the analyses. Questions that expanded on an "other" response, or that were open-ended questions, such as "type of pesticide used in the field," were excluded from analysis. In Table 3.1, the "Type" column denotes whether a variable was originally used as a question in the Yuma Study, or whether a variable was created for the additional analyses in this report. (A variable is defined as the set of participant responses for a specific question that are assigned codes for analysis.) The "Brief Description" is used to identify the questions in subsequent tables. The "Extended Description" includes the full statement of the question. "Principal child" and "participant" are used interchangeably in Table 3.1 to refer to the principal participant child.

Table 3.1 Questionnaire Variables from the Yuma Study Used in Data Mining Analyses, Sorted by the Questionnaire Order

Type[a]	Name	Brief Description	Extended Description
Original	AGE	Age of principal child	Age of principal child calculated from date of birth
Original	SEX	Child's gender	Gender of principal child
Original	HEIGHT	Child's height (inches)	Measurement of principal child's height without shoes (inches)
Original	WEIGHT	Child's weight (lbs)	Measurement of principal child's weight without shoes or other heavy articles (lbs)
Original	SCHOOL	Child's school	School where principal child attends
Original	GRADE	Child's grade	What grade is the principal child in?
Original	ETHNIC	Child's ethnic and racial background	Child's ethnic and racial background
Original	LIVEYEAR	Number of years child lives at this address	Number of years child lives at this address
Original	LIVEAREA	Children/respondent lives in area part-time	Children/respondent live in area < 10 months/year
Original	PEOPLIVE	Number of people in household including participant	Number of people in household including participant
Original	YOUNGSIB	Number of children in household $\leq$ 11 years old	Number of additional children in household $\geq$ 2 years and $\leq$ 11 years old?
Original	CHEMINHS	Pesticides used inside home last month?	Were chemicals to control insects used inside the house during the last month?
Original	WHOCHEMI	Who applied pesticides inside the house?	Who applied chemicals inside the house?
Original	LIVINGRM	Living room treated with pesticides?	Was living room treated with pesticides?
Original	FAMILYRM	Family room treated with pesticides?	Was family room treated with pesticides?
Original	DININGRM	Dining room treated with pesticides?	Was dining room treated with pesticides?
Original	KITCHEN	Kitchen treated with pesticides?	Was kitchen treated with pesticides?
Original	BATHROOM	Bathroom treated with pesticides?	Was bathroom treated with pesticides?
Original	BEDROOM	Bedroom treated with pesticides?	Was bedroom treated with pesticides?
Original	CHILDBED	Child's bedroom treated with pesticides?	Was child's bedroom treated with pesticides?
Original	BASEMENT	Basement treated with pesticides?	Was basement treated with pesticides?
Additional	NRMSPRYD	Number of rooms sprayed last month	Number of rooms in house sprayed with pesticides in past month

Type[a]	Name	Brief Description	Extended Description
Original	OTHERRM	Other rooms treated with pesticides?	Were other rooms in the house treated with pesticide?
Original	OFTCHEMI	How often is home treated for pests?	How often is participant's home treated for pests?
Original	CHEMOUTH	Pesticides used outside home last month?	Were chemicals to control insects used on the exterior or foundation of the house during the last month?
Original	WHOCHEMO	Who applied pesticides outside house?	Who applied chemicals outside house?
Original	FARFIELD	Distance between home and agricultural field	How far is participant's home from a field where crops are grown?
Original	CLOSEAPP	Distance between home and nearest application of pesticides	In past month, how close to participant's home was the nearest application of agricultural or gardening chemicals?
Original	GPS	Distance between home and field using GPS	How far is participant's home from a field where crops are grown?
Original	WHEEL	Distance between home and field - rotary wheel	Distance from home to field measured with rotary wheel - categories
Original	HOWCHEMO	How pesticides were applied to fields	How were agricultural chemicals applied to field close to participant's home?
Original	WHNCHEMO	Last time field treated with pesticides?	When was the last time the field was sprayed or treated with pesticides?
Original	VEGGIES	How often child eats local fresh fruit/veg?	During the year, how often does principal child eat locally grown fresh fruits or vegetables?
Original	WASHVEGI	How often wash local fresh fruit/veg before eating?	How often are the locally grown fresh fruits and vegetables washed before they are eaten?
Original	HOURAWAY	Number hours/wk child not at home	During school year, about how many hours per week does principal child spend away from home?
Additional	CHLDTM1	Child spends time in another home?	Principal child routinely spends time away from home – in another home
Additional	CHLDTM2	Child spends time at day care center?	Principal child routinely spends time away from home – at day care center
Additional	CHLDTM3	Child spends time at school?	Principal child routinely spends time away from home – at school
Additional	CHLDTM4	Child spends time at sport event?	Principal child routinely spends time away from home – at sport event
Additional	CHLDTM5	Child spends time playing in field?	Principal child routinely spends time away from home – playing in field
Additional	CHLDTM6	Child spends time playing in irrigation water?	Principal child routinely spends time away from home – playing in irrigation water
Additional	CHLDTM7	Child spends time playing outside?	Principal child routinely spends time away from home – playing outside
Original	WHERTIME	Room where child spends most awake time	Room where principal child spends most of their awake time
Original	SPRAYFLD	Child in yard when fields sprayed or dusted?	Does principal child play outside in the yard when the fields are sprayed or dusted?
Original	WATERSR1	Drinking water source - public/commercial	Source of drinking water in participant's home is public/commercial

Type[a]	Name	Brief Description	Extended Description
Original	WATERSR2	Drinking water source - private well	Source of drinking water in participant's home is private well
Original	WATERSR3	Drinking water source - cistern	Source of drinking water in participant's home is cistern
Original	DADWORK	Is the father currently employed?	Is the father currently employed?
Original	NCATWRKD	Father's occupation -- categories	Father's occupation -- categories
Additional	DADPEST	Are pesticides used where father works?	Are pesticides used where father works? -- categories
Additional	DADCON2	Father's occupation -- location and pesticide use	Does father work indoors or outdoors and with or without pesticides?
Original	MOMWORK	Mother now employed (not as housewife)?	Is the mother currently employed?
Original	NCATWRKM	Mother's occupation -- categories	Mother's occupation -- categories
Additional	MOMPEST	Are pesticides used where mother works?	Are pesticides used where mother works? -- categories
Additional	MOMCON2	Mother's occupation -- location and pesticide use	Does mother work indoors or outdoors and with or without pesticides?
Original	ADLTPEST	Non-parent in home works where pesticides used?	Is there another person living in the house (other than parent) who works in a place where pesticides are used?
Original	ADTPSWK	Non-parent in home works where pesticides used?	Any adult in household works where pesticides used?
Original	NUMADLTS	Number of additional adults in home	Number of non-parent adults in home working with pesticides
Original	CHILDFLD	Child worked in fields last month?	Has principal child been to the work field(s) during past month?
Original	WHENFILD	Last time child was in work field	When was the last time principal child was in the work field?
Additional	WHERMD1	Family med care at private medical clinic	Where principal child's family receives medical care – private medical clinic
Additional	WHERMD2	Family med care at health dept clinic	Where principal child's family receives medical care – local health department clinic
Additional	WHERMD3	Family med care at other med clinic	Where principal child's family receives medical care – other medical clinic
Additional	WHERMD4	Family med care in Mexico	Where principal child's family receives medical care – Mexico
Additional	WHERMD5	No access to medical care	Where principal child's family receives medical care – no access
Additional	WHERMD6	Family med care at other place	Where principal child's family receives medical care – at other facility
Additional	WHERMD7	Family med care - do not know	Where principal child's family receives medical care – do not know
Original	POISON	Anyone treated for pesticide poison?	Has anyone in the household been treated for pesticide poisoning in past year?
Original	HOWCHILD	Child's health in general	Description of principal child's health in general

Type[a]	Name	Brief Description	Extended Description
Original	LICE	Child treated for head lice past six months?	Has principal child been treated for head lice in past six months?
Original	INSURED	Is child covered by medical insurance?	Is principal child covered by medical insurance?

[a] Original variables existed in the data set provided from the Yuma Study. Additional variables were created based on the original variables.

Code values were reassigned for non-responses, conditional questions, and to create an underlying continuum of potential exposure. See Appendix G for information on coding schemes and additional variables created.

The chemical/metabolite measurements for the urine, house dust, and school dust samples that were used in the data mining analyses were analyzed as molar-weighted sums (Table 3.2). Appendix F includes a list of all the chemicals and metabolites measured in the Yuma Study, the specific chemicals included in each sum, and an example of how the sums are calculated. For the urinary metabolite sums, the log of the sum was used as the dependent variable.

Table 3.2 Analytical Measurement Variables from the Yuma Study Used in Data Mining Analyses

Name	Description[a]
Urine from Child	
LWETHSUM	Log of weighted sum of DEP, DETP, and DEDTP (adjusted for creatinine) [b]
LWMETHSM	Log of weighted sum of DMP, DMTP, and DMDTP (adjusted for creatinine) [c]
Household Dust	
WCHDNSUM	Weighted sum of alpha-chlordane and gamma-chlordane
WCHLPYRF	Weighted chlorpyrifos
WCYPRMET	Weighted cy-permethrin
WDDSUM	Weighted sum of 4,4'DDD, 4,4'DDE and 4,4'DDT
WDIAZNON	Weighted diazinon
WDUSTBAL	Weighted sum of dust analytes except chlorpyrifos, diazinon, permethrins, and o-phenylphenol
WDUSTSUM	Weighted sum of all dust analytes
WOPBAL	Weighted sum of OP pesticides except chlorpyrifos and diazinon
WOPHNYLP	Weighted o-phenylphenol
WOPSUM	Weighted sum of OP pesticides
WPERMSUM	Weighted sum of cis-permethrin and trans-permethrin

Name	Description[a]
School Dust	
SWCHDNSM	Weighted sum of alpha-chlordane and gamma-chlordane
SWCHLPYR	Weighted chlorpyrifos
SWCYPRME	Weighted cy-permethrin
SWDDSUM	Weighted sum of 4,4'DDD, 4,4'DDE and 4,4'DDT
SWDIAZNO	Weighted diazinon
SWDSTBAL	Weighted sum of dust analytes except chlorpyrifos, diazinon, permethrins, and o-phenylphenol
SWDUSTSM	Weighted sum of all dust analytes
SWOPBAL	Weighted sum of OP pesticides except chlorpyrifos and diazinon
SWOPHNYL	Weighted o-phenylphenol
SWOPSUM	Weighted sum of OP pesticides
SWPERMSM	Weighted sum of cis-permethrin and trans-permethrin

[a] See Appendix F for definition of weighted sums.
[b] DEP – diethylphosphate, DETP – diethylthiophosphate, DEDTP – diethyldithiophosphate
[c] DMP – dimethylphosphate, DMTP – dimethylthiophosphate, DMDTP – dimethyldithiophosphate.

3.3.3 Stage 2 – Review of Basic Relationships

In Stage 2, relationships between questionnaire and analytical measurement data were reviewed. This stage was exploratory rather than inferential and helped determine the sets of variables to be analyzed in Stage 3. As the basic analyses were performed and seeming inconsistencies in the relationships appeared, the data were reviewed. Stage 2 included evaluating simple indicators of high exposure levels, identifying relationships between questionnaire variables, and refining the group of participants to be included in the Stage 3 analyses.

3.3.4 Stage 3 – Classification Approach

The Stage 3 analyses were performed using the data mining technique Classification and Regression Trees (CART). This method divides the study population into subsets of participants where the between-subset variability of the dependent variable (e.g., LWETHSUM from Table 3.2) is maximized and the within-subset variability is minimized. The predictors or independent variables (questions and dust measurements in this study) can be nominal, ordinal, or continuous in nature and are the basis for defining the subsets. CART attempts to identify a model of predictors and their interactions that optimally classify subjects by the dependent variable, in this case, the child's measured exposure level for a specific metabolite. The output from CART is a classification map, or tree, that describes the subsets of the study population in terms of the dependent variable values and provides characteristics of the subsets in terms of the predictors and the predictors' values. This is analogous to a regression equation without a functional form. The predictors selected in the CART analyses can help differentiate children's pesticide exposure levels as measured by the molar-weighted DAP sums.

Details of the methodology for the data mining approach can be found in Appendix G.

4.0 RESULTS AND DISCUSSION

4.1 Introduction

The objective of this project is to evaluate questions that are potential indicators of pesticide metabolite levels in children's urine and to identify the more useful questions as input for future study design. The evaluation reviewed relationships between questions and exposure measurements under two approaches:

- A literature review of previous exposure studies to summarize the existence of such quantitative and qualitative relationships, and
- An analysis of a recent children's pesticide exposure study in Yuma, Arizona, which included questionnaires and measurements.

As work proceeded, it became obvious that environmental measurements were also useful in completing the link between questions and metabolite levels. The results from each approach are described and discussed in this section. A summary of the results is also presented in section 2.

4.2 Literature Review

Most of the pertinent studies on children's exposure to pesticides began in the 1990's, a much shorter period of study than for adults. The publications reviewed were those published through early 2003. Multiple searches of the literature resulted in over 100 citations (section 3.2). The abstracts and publications were reviewed against the first set of criteria, which required a pertinent publication to:

- address the pesticide exposure of children,
- have collected monitoring samples, preferably urine, and
- indicate the use of a survey or questionnaire in the study.

Of the publications meeting the first set of criteria, 64 were reviewed against a second set of criteria, which required a pertinent publication to:

- study pesticide exposure,
- describe relationships between questions and measurements from monitoring samples, and
- include children as part of the population studied.

These criteria categorized 20 of the 64 publications as "relevant" (Table A.1) and the remaining 44 publications as "not applicable" (Table A.2). Twenty publications of the relevant publications were peer-reviewed journal articles. Four of the twenty relevant publications were subsequently categorized as not applicable. Bradman (1997), Mills (2001), O'Rourke (2000), and Thompson (2003) included study designs that were pertinent to this review; however, either the particular publication did not include the required relationship information, or the study was a pilot that contained only a small number of subjects. The

Bradman (1997) and Mills (2001) publications had sample sizes less than 10. The O'Rourke (2000) and Thompson (2003) publications included information on pesticide metabolites in children's urine, but did not attempt to draw associations between this information and questionnaire data. Four Masters' theses were subsequently added to the relevant publications list. Two of the theses produced journal articles that are among the relevant publications, and were included because they provided details not available in the articles: the Carrel (1996) thesis was published as Loewenherz (1997), and was expanded upon in Lu (2000); the Koch (1999) thesis was published as Koch (2002). The other two Masters' theses were included because their findings have not been published in the peer-reviewed literature: the Grossman (2001) thesis was based on the same field study reported on by Curl (2002) and Thompson (2003), but the analysis conducted by Grossman was not included in either of these publications. The Krinsley (1998) thesis work has not been published elsewhere. Future references to the relevant publications list will denote the 20 publications from which relationship information was extracted. These 20 publications covered aspects of 14 different exposure studies. Appendix A includes references for all publications reviewed.

Results from the literature review are presented as information on each "relationship" between a question and exposure measurement described in the relevant publications. Relationship, as used in this report, is defined as a systematic correspondence between the values of two variables from an exposure study, that is, questionnaire responses and analytical measurements. This correspondence may or may not be statistically significant. As the review of the publications progressed, the scope of relationships considered for this report was expanded to include relationships with environmental media as well as biomarkers to enhance the information base relating to potential exposure pathways. When reviewing individual relationships to ensure comparability, the reader should be cognizant of study and analysis particulars. Unless stated otherwise in the Results and Discussion section, significant and statistically significant will be interchangeable.

In the process of extracting pertinent relationship information, each publication was reviewed several times. Since the publications were not consistent in the manner or level of information provided for the relationships, a structure was developed to capture the variety of information available. The objective of this review process was to ensure that the relationship information was extracted correctly, as the authors intended it to be interpreted, and to make few if any assumptions. In a few instances, authors were contacted to clarify information presented in the publications.

4.2.1 Publications Reviewed for Relationships

The studies on which the 20 relevant publications are based were assigned abbreviated citation references to be used in this and other sections of the report. The studies as used in the publications are briefly described with information about the study's location, population, media, pesticides measured, and types of questions asked (Table 4.2.1). Some studies generated more than one publication. Related publications and a study number are included for those instances.

Table 4.2.1 Brief Descriptions of the Studies Included in the 20 Relevant Publications

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Adgate 2001 STUDY 1[c]	Minnesota: Urban (Minneapolis/St. Paul) and non-urban areas (Rice and Goodhue counties)	102 children 3-13 years old -- Preferences were for households with more frequent pesticide use, more than 1 eligible child, use of a private well in non-urban areas, children having greater potential for recent exposure to target pesticides.	Urine	Metabolites: 1-naphthol, atrazine mercapturate, malathion dicarboxylic acid, 3,5,6-trichloro-2-pyridinol.	Characteristics of the participating child and housing, usual frequency of activities over a period of a month or year, detailed (daily) time and location information of activities for the child, and information on less than daily activities during the monitoring period.	Sexton 2003
Aprea 2000 STUDY 2	Tuscany, Italy	195 children 6-7 years old -- Children were enrolled in elementary schools in Siena, Italy, which does not have major industries. Population is employed mostly at banks, hospitals, universities, or as shopkeepers, and professionals.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP, DEDTP	Lifestyle and dietary habits -- sex, date of birth, weight, height, school, class, father and mother's occupations, illness and hospitalization of child, existence of garden or vegetable garden, existence of ornamental plants in house, purchase of cut flowers for the house, domestic animals in house, use of pesticides inside or outside house, food and drink ingested day before urine sample, and ate lunch at school. Diet, parent's occupation, height, weight and height/weight ratio were used for qualitative classification of population.	

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Azaroff 1999 STUDY 3	Rural El Salvador	103 farmer households and family members at least 8 years old -- Families were recruited from five agricultural communities who lived there during planting season. Household members who lived in the home during planting season and were able to answer questions were included.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP, DEDTP	Application of pesticides to crops, age and sex of household members, laundry practices, field work, and pesticide use for the house.	
Carrel 1996[d] STUDY 4	Washington (Douglas and Chelan counties)	88 children no more than 6 years old -- Two family types were selected: pesticide applicator in family living near sprayed orchard, and family with no pesticide applicator living further from orchard. One child selected per family.	Urine	Metabolites: DMP, DMTP, DMDTP	Occupational and residential pesticide use, cleaning activities, laundry practices, protective equipment use, proximity to spray sites, and child activity.	Published as Loewenherz 1997; expanded in Lu 2000; analysis of diethyl metabolites in Fenske 2002

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Curl 2003 STUDY 5	Seattle, Washington	43 children 2-5 years old – Children were recruited based on whether their juice, fresh fruit, and fresh vegetable consumption was either nearly all organic or nearly all conventional.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP	Age and weight of child, parental age, and occupation, annual family income, home ownership, length of time at the current residence, housekeeping practices, residential pesticide use (in the home, on the home structure, in the garden, on the lawn, and on pets), time since last pesticide application and who applied the pesticide, child behaviors: thumb-sucking, hand washing, hand-to-mouth activity, and amount of time spent outside of home. Food diary for child with type and amount of food and beverage and whether each item was organic or not. Food diary was used for classification of child's diet.	
Curl 2002 STUDY 6	Washington	218 farm-worker households in 24 agricultural communities -- One farm-worker actively involved in field work or pesticide application and one 2-6 year old child were sampled from each household.	Urine, dust	Pesticides: azinphosmethyl, malathion, methyl parathion, phosmet, chlorpyrifos, diazinon Metabolites: DMP, DMTP, DMDTP, DEP, DETP	Types of agricultural job tasks, occupational pesticide exposure, perceived health effects of pesticide exposure, occupation and personal protective practices, and demographics.	Grossman 2001
Fenske 2002 STUDY 4	Central Washington	75 homes and 109 children up-to-6-years old -- Three family types were selected: pesticide applicator in family living near sprayed orchard, pesticide applicator in family living further from orchard, and no pesticide applicator in family living further from orchard.	Urine, dust, dermal wipe	Pesticides: chlorpyrifos, ethyl parathion. Metabolites: 3,5,6-trichloro-2-pyridinol, 4-nitrophenol.	Occupational and residential pesticide use, hygienic and housekeeping practices, child behavior and activity, and proximity of home to pesticide-treated fruit orchard.	Carrel 1996, Lu 2000, Loewenherz 1997

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Grossman 2001[d] STUDY 6	Lower Yakima Valley, Washington	148 households with children 2-6 years old -- Hispanic farm-worker households were selected from For Healthy Kids, a community intervention study of take-home pesticide exposures.	Dust	Pesticides: azinphosmethyl	Sociodemographic characteristics and acculturation, agricultural tasks, knowledge about pesticides and related health effects, perceived exposure to pesticides, workplace facilities, and work and home practices related to pesticide exposure.	Curl 2002
Koch 2002 STUDY 7	Central Washington	44 children 2-5 years old -- Households were recruited from a Women, Infants and Children (WIC) clinic in a fruit tree production region. One child per family was selected.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP	Characteristics of the study child, parental occupations, household pesticide use, and children's activities	Koch 1999
Koch 1999[d] STUDY 7	Central Washington	44 children 2-5 years old -- Households were recruited from a Women, Infants and Children (WIC) clinic in a fruit tree production region. One child per family was selected.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP	Characteristics of the study child, parental occupations, household pesticide use, and children's activities	Koch 2002
Krinsley 1998[d,e] STUDY 8	Arizona, including US-Mexico border	179 households that were full-time Arizona residents and were a subset of the Arizona NHEXAS study. The focus was on high risk subgroups of minorities, children, and US-Mexico border residents.	Urine	Pesticides: chlorpyrifos Metabolites: 3,5,6-trichloro-2-pyridinol	Health status, occupation, pesticide use characteristics, home characteristics, demographic information, behavior, time-activity, and daily diet diaries.	

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Loewenherz 1997 STUDY 4	Washington (Douglas and Chelan counties)	88 children no more than 6 years old -- Two family types were selected: pesticide applicator in family living near sprayed orchard, and family with no pesticide applicator living further from orchard. One child selected per family.	Urine	Metabolites: DMP, DMTP, DMDTP	Occupational and residential pesticide use, cleaning activities, laundry practices, protective equipment use, proximity to spray sites, and child activity.	Carrel 1996, Fenske 2002, Lu 2000
Lu 2001 STUDY 9	Seattle, Washington	110 children 2-5 years old -- Families recruited from clinic and outpatient waiting rooms in two communities -- an urban, densely-populated one with lower to middle income families, and a suburban one with middle to upper income families. One focus child was selected from each family.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP, DEDTP	Characteristics of the child, parental occupation and family income level, home ownership status, length of time at current residence, housekeeping practices, residential pesticide use regarding pets, lawn or vegetable/flower garden, professional application of pesticides in last 6 months, which pesticide products were applied, and child's activities and behaviors.	
Lu 2000 STUDY 4	Central Washington	109 children from 9 months to 6 years old from 76 households -- Three family types were selected: pesticide applicator in family living near pesticide-treated orchard, farm-worker in family living near pesticide-treated orchard, and no pesticide applicator in family living > .25 mi from pesticide-treated orchard.	Urine, dust, dermal wipe	Pesticides: azinphosmethyl, phosmet. Metabolites: DMP, DMTP, DMDTP.	Occupational and residential pesticide use, hygienic and housekeeping practices, child behavior and activity, and proximity of home to pesticide-treated fruit orchard.	Carrel 1996, Fenske 2002, Loewenherz 1997

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
McCauley 2003 STUDY 10	Hood River, Oregon	24 fruit-tree orchard agricultural families with at least one adult member working in an orchard full time, and with at least one 0-7 year old child; four control families.	Dust	Pesticides: azinphosmethyl, chlorpyrifos, malathion, phosmet, diazinon, parathion	Demographics, agricultural work practices of all adult family members residing in the home, self-reported protective practices at work and upon coming home, residential pesticide use, a household pesticide inventory, land use and proximal crop information, child play locations, and precautions taken by family during pesticide spraying events.	
McCauley 2001a STUDY 11	Oregon (Washington and Hood River counties)	96 families with preschool children -- Families were recruited from children enrolled in Migrant Head Start centers.	Dust	Pesticides: azinphosmethyl	Demographics, agricultural work practices of all adult family members residing in the home, self-reported protective practices at work and upon coming home, residential pesticide use, a household pesticide inventory, and land use and proximal crop information.	
Royster 2002 STUDY 12	Imperial County, California	20 children 12-18 months old – Children were recruited during well-child visits at clinics, when due for their first MMR (measles, mumps, rubella) vaccination, without certain health issues.	Urine	Metabolites: DMP, DMTP, DMDTP, DEP, DETP, DEDTP	Family's occupational pesticide exposure, the child's and family's health histories, pesticide usage, proximity to agricultural fields, location of residence, source of drinking water, history of smoking within household, and demographic characteristics.	

Citation Reference[a]	Location	Population	Media Studied	Pesticides Studied[b]	Type of Questions Asked	Related Work
Sexton 2003 STUDY 1	Minnesota: Urban (Minneapolis/St. Paul) and non-urban (Rice and Goodhue counties) areas	102 children 3-13 year-olds -- Preferences were for households with more frequent pesticide use, more than 1 eligible child, use of a private well in non-urban areas, children having greater potential for recent exposure to target pesticides.	Urine, dust, hand rinse, soil	Pesticides: chlorpyrifos, diazinon, malathion, atrazine. Metabolites: malathion dicarboxylic acid, 3,5,6-trichloro-2-pyridinol	Occupant characteristics, household characteristics, household pesticide use and occupant activities. Characteristics of the participating child and housing, usual frequency of activities over a period of a month or year, detailed (daily) time and location information and activities for the child, and information on less than daily activities during the monitoring period.	Adgate 2001
Shalat 2003 STUDY 13	Rio Bravo, Texas	52 children 7-53 months old -- 29 households were selected from an agricultural community on the US-Mexico border.	Urine, dust, hand rinse, soil	Pesticides: azinphosmethyl, chlorpyrifos, demoton O, demoton S, diazinon, ethion, fenithrothion, ethyl parathion, methyl parathion. Metabolites: DMP, DMTP, DMDTP, DEP, DETP, DEDTP	Medical information, occupational information, time/activity information, children's hand-to-mouth activities, diet, residential pesticide use, and pets or animals in the household.	
Simcox 1995 STUDY 14	Central Washington	59 households with at least one child 1-6 years old -- Households included reference families, and agricultural families where at least one family member living in the home was employed as an orchardist, field worker, and/or pesticide applicator.	Dust, soil	Pesticides: azinophosmethyl, chlorpyrifos, ethyl parathion, phosmet	Occupational pesticide use, residential and agricultural pesticide use in past 6 months, proximity of home to orchards, protective practices, and family hygiene practices.	

[a] See Table A-1 (Appendix A) for citations.
[b] DEP – diethylphosphate, DETP – diethylthiophosphate, DEDTP – diethyldithiophosphate
DMP – dimethylphosphate, DMTP – dimethylthiophosphate, DMDTP – dimethyldithiophosphate.
[c] Some studies generated multiple publications and are identified with the same study number.

[d] Masters theses related to publications in the initial relevant list.
[e] Data used for the Krinsley thesis are available at EPA's Human Exposure Database System (HEDS) web site at: http://www.epa.gov/heds/index.htm under the NHEXAS Arizona Study.

4.2.2 Description of Relationship Information

4.2.2.1 Content

Detailed information was extracted for each relationship to provide a useful reference tool for diverse research needs. A simple database was created using MS Excel to capture the relationship information presented in Sections 4.2.4, 4.2.5, and 4.2.6, and in Appendices B, C, and D. The types of information included are descriptive, general analysis, and statistical analysis (Table 4.2.2). The data fields under the analysis types of information refer to the results of a statistical analysis or to the groups compared in the statistical analysis.

Table 4.2.2 Information Extracted from Relevant Publications for Each Relationship

Type of Information	Data Fields[a]
Descriptive	
	Citation reference
	Question asked
	Sample medium
	Chemical measured
	Type of measurement, e.g., concentration or loading
	Log transformation indicator
	Subpopulation included in the analysis
	Type of statistical analysis performed
	Groups compared in the analysis, if relevant
	Significance indicator for analysis
	Comments about the chemical measurement
Analysis: General	
	p-value for the statistical analysis
	p-value for model or predictor indicator
	Comments about the analysis
Analysis: Statistics	
	Units of chemical measurement
	Geometric mean
	Geometric standard deviation
	Median
	Mean
	Standard deviation
	Percent detectable measurements
	Number of subjects
	Odds ratio (from logistic regression)
	Confidence interval (95% level for either Odds Ratio or Beta)

Type of Information	Data Fields[a]
	Beta (coefficient from regression analysis)
	R^2 -- square of multiple correlation coefficient from regression analysis

[a] Analysis refers to statistical analysis unless otherwise noted.

The available statistical parameters differ across publications and relationships. Relationships were included in the database based on the type of relationship measured and the types of information available. Two types of relationships were not included in the database: relationships for which no information on a statistical analysis was provided even though statistical parameters at a group level (e.g., means by age group) were provided, and relationships where the analysis did not fit the project's objective (e.g., a relationship between two questions). As much of the pertinent information as possible was extracted for each relationship from the publications for inclusion in the database.

The descriptive fields in the database (Table 4.2.2), and the study information (Table 4.2.1) set the context for each relationship that was evaluated because a study's design or the study subgroups compared in a statistical analysis can affect the significance of the relationship between the question and the measurement. The general and statistical analysis fields in the database allow for additional evaluation of a question's usefulness in understanding exposure-related activities and their potential impact. For example, knowing that a question showed a statistically significant relationship to a particular type of measurement in two separate relationships provides one type of information. Also knowing that in one of the relationships the median for group A was greater than the median for group B, and in the other relationship the median for group B was greater than the median for group A provides a different type of information. The inconsistent relationship between the medians of the two groups is a cue for the reader to consider the possibility of confounding factors (e.g., related to design) in the analyses or to recognize that the usefulness of the question in predicting exposure level may not yet be adequately proven. The database of information, as included in Appendices, B, C, and D, allows the reader to review the relationships from these perspectives.

4.2.2.2 Organization

Each relationship was assigned a unique ID number that will be shown in the tables describing the relationships. This ID number was used primarily for tracking and for preparing the information in table format. Because the breadth of information extracted for the relationships could not easily be presented in a single table format, the relationship information was grouped into three types of tables, an overview, details, and comments, which are included in Appendices B, C, and D, respectively. The ID number can be used to match information between Appendices C and D.

Another level of organization for the relationships was introduced at the question level. The publications differ in how, and to what extent, the questions are described. Some provide the full question, and some provide an abbreviated or generalized description of the question. To analyze their usefulness, question descriptions that at least implied the same question are grouped together, and a question number, e.g., Q102, has been assigned to each question phrasing for ease of reference in other tables. Thus, for each relationship, an abbreviated question phrasing was assigned. For example, the abbreviated question phrasing or description "inside treated" includes the following questions:

- pesticide use inside
- pesticide used inside in past 6 months
- Was there indoor pesticide application in past 6 months?
- In the past 6 months were any chemicals for the control of fleas, roaches, ants or other insects used inside this house/apartment?

Judgments were made regarding the level of abbreviated question descriptions to use. Since, in a few instances, the specificity of the question may affect the comparison of relationships, the description of the question as it is presented in the publication is included in Appendix D with supplemental information about the relationship. Reviewing the question descriptions allows the reader to evaluate the summary results and any influence from the question groupings.

A third level of organization arranges the question phrasings (the abbreviated question descriptions) into 14 question categories, and three risk factor groups for presentation and discussion purposes (Table 4.2.3). These groupings provide the organization of information and relationships in sections 4.2.4, 4.2.5, and 4.2.6, and in Appendices B, C, and D.

Table 4.2.3 Distribution of Relationships Across Risk Factor Groups and Question Categories[a] of Questions Used to Organize Sections 4.2.4, 4.2.5, 4.2.6, Appendix B, Appendix C, and Appendix D

Risk Factor Group	Question Category		Relationships	
Description	#	Description	N	%
Source	1	Residential pesticide use[b]	100	17
Source	2	Household characteristics[b]	73	12
Source	3	Residential sources (environmental measures)	13	2
Source	4	Household occupation	115	19
Source	5	Residential proximity to agricultural fields	72	12
Source	6	Residential location	14	2
Behavior	7	Subject's personal characteristics	78	13
Behavior	8	Child's behaviors	20	3

Risk Factor Group	Question Category		Relationships	
Description	#	Description	N	%
Behavior	9	Dietary behaviors	16	3
Behavior	10	Family hygiene practices	81	13
Behavior	11	Smoking-related activities	4	1
Behavior	12	Work exposure/practices	4	1
Other	13	Related exposure levels	5	1
Other	14	Health	8	1
		Total	603	100

[a] Based on counts in Appendix B tables.
[b] See note in the following paragraph regarding relationships from Sexton (2003).

Sexton (2003) evaluated many relationships between questions in the residential pesticide use and household characteristics categories, and measurements of atrazine, diazinon, malathion, and chlorpyrifos in personal air, indoor air, outdoor air, solid food, beverages, dust, soil, and urine under several statistical analysis scenarios. The majority of the relationships analyzed were not statistically significant. Since these relationships represented a large number of relationships for which no additional statistical information is provided, they were not included in the relationship database. The reader should be cognizant of this exclusion because it affects the percentages of statistically significant versus non-significant results in subsequent summary tables. However, if included, the large number of non-significant analyses would give more weight to the results from this publication than perhaps reasonable. Each table affected by this exclusion will be footnoted for the reader's awareness. All statistically significant relationships, and any non-significant relationships specifically noted in the publications' tables or text, were included in the database.

Six question categories had the largest number of relationships: residential pesticide use, household characteristics, household occupation, residential proximity to agricultural fields, subject's personal characteristics, and family hygiene practices. These categories are likely considered the most appropriate questions for the type of exposures studied because of expected or proven relationships. The fact that these categories have more relationships than the other categories may provide more credence overall to predictors selected from these categories. That judgment will specifically depend on the number of relationships available for a given combination of question and chemical or metabolite. Potential predictors from the other eight categories may also be useful, but have not been tested enough to make adequate judgments.

The number of relationships for the urine and dust media overwhelms the number from any other medium, with twice as many relationships for urine as for dust (Table 4.2.4).

Table 4.2.4 Distribution of Relationships across Question Categories and Mediums Measured[a]

Question Category		Number of Relationships, by Medium							
#	**Description**	**Urine**	**Dust**	**Indoor Air**	**Outdoor Air**	**Personal Air**	**Soil**	**Solid Food**	**All Media**
1	Residential pesticide use[b]	81	8	2	2	4		3	100
2	Household characteristics[b]	54	18	1					73
3	Residential sources (environmental measurements)	5	8						13
4	Household occupation	48	59				8		115
5	Residential proximity to agricultural fields	30	42						72
6	Residential location	13	1						14
7	Subject's personal characteristics	80							80
8	Child's behaviors	18							18
9	Dietary behaviors	16							16
10	Family hygiene practices	33	48						81
11	Smoking-related activities	4							4
12	Work exposure/practices	1	3						4
13	Related exposure levels	5							5
14	Health	8							8
	Total	396	187	3	2	4	8	3	603
	Percent of Total	65.7	31.0	0.5	0.3	0.7	1.3	0.5	

[a] Based on counts in Appendix B tables.
[b] See the paragraph immediately following Table 4.2.3 regarding relationships from Sexton (2003).

4.2.2.3 Assumptions and Caveats

Great care was taken and quality assurance was applied when extracting the relationship information from the publications. Each publication was reviewed several times to identify all hypothesized relationships noted. The ID# for each relationship was noted on a copy of the publication for cross-checking and the information extracted was reviewed by more than one person. The intent was to extract information without assumptions or interpretation. There are a few situations where judgments or assumptions were made to provide as much, and as consistent, information as possible (Appendix D). Relationships mentioned in a publication's text, but not specifically included in tables, were also extracted.

In several publications, questions were identified as part of the study's interview process; however, no results from analyzing relationships were mentioned. To determine the reason for the absence, and to glean any additional information for the database, an author of the publication was contacted. In most instances, the relationships in question were excluded from the publication because they were not significant or were to be included in future publications. In four instances, these contacts led to the inclusion of four Masters' theses as relevant citations: Carrel (Loewenherz) (1996), Grossman (2001), Koch (1999), and Krinsley (1998). Complete copies of the Grossman and Krinsley theses were reviewed. Parts of the Koch and Carrel theses were made available for this report in response to specific questions in the related publications.

Significance levels for the statistical analyses are reported in various ways, even within a publication. For example, p-values may be specified as a value ($p = 0.042$) or as an interval ($p < 0.05$). Sometimes the significance level is noted only as an indicator, that is, significant, not significant, marginally significant, or as a trend. Since knowing the p-value rather than a general indicator of significance allows the reader to make decisions based on their research objectives, the p-values were added to the database as a separate field. In cases where the significance indicator rather than the p-value is given, the publication was reviewed to identify the p-value used as the critical value for statistical significance. In all of the publications, the p-value for identifying significant relationships was 0.05. When the marginally significant or trend indicator was noted, the critical values are either 0.10 or 0.20. When no p-value is noted for a relationship, one was added based on the publication's significance indicator. For example, if the publication's critical value for significance is $p = 0.05$, $p > 0.05$ was noted in the database for a relationship identified as not significant. If the publication's critical value for being marginally significant was $p = 0.10$, $p > 0.10$ is noted in the database for a relationship identified as not marginally significant.

The extent of inferences that can be made from the relationships presented must be taken into account. Most of the studies conducted were convenience samples. Analyses from such studies are descriptive of the particular group sampled, and may or may not generalize to similar populations. The value of these relationships, however, is that they identify potential trends that may exist in the populations. When evaluating the effectiveness of a question for a particular research situation, it is also important to review and understand the similarities and differences in the samples taken, the type of measurements taken and analyzed, and the subgroups compared across the relationships available for the question. The reader may need to review the pertinent publications for some of these details.

4.2.3 Description of Relationships Presented

The amount and variety of information available across the relationships made it difficult to create a presentation format that was easy to read without being burdensome in other respects. The selected formats are more compact, but require more introduction to, and scrutiny by, the reader. This section briefly describes the content and organization of the tables in the upcoming sections, and gives an introduction to the related tables in Appendices B, C, and D.

The question categories (Table 4.2.3) provide the framework for the presentation and discussion of the results from the literature review. Questions for each of the three risk factors are discussed in separate sections. Source relationships are presented in section 4.2.4, behavior relationships are presented in section 4.2.5, and other relationships are included in section 4.2.6. The questions included under each risk factor and question category can be found in Appendix E. For each question category, three types of summary tables are presented as part of the evaluation and discussion. These tables describe the effectiveness of the questions in differentiating exposure levels by describing the extent of statistically significant relationships for each question and metabolite/chemical combination.

The first table type, "a," for each question category, e.g., Table 4.2.6.**a**, lists the coded names and descriptions for the chemicals/metabolites with significant relationships in the question category. Thus, of all the chemicals/metabolites measured in relationships with questions from this category (Tables B.3.1.1.a-g), only the 11 listed in Table 4.2.6.a had significant relationships. The second table type, "b," e.g., Table 4.2.6.**b**, shows the number and percentage of significant relationships by medium for the category. Thus, in Table 4.2.6.b, there are three significant relationships for ATZ (atrazine) in personal air and residential pesticide use questions. Four relationships for personal air were found for this category, and 75% of the relationships are statistically significant (Table B.3.1.1.f). The third table type, "c," e.g., Table 4.2.6.**c**, lists each question/medium/chemical-metabolite combination for which a majority (>50%) of the relationships are either significant or marginally significant. Thus, in Table 4.2.6.c, the question Q119-outside treated, overall has statistically significant relationships for MDA and TCPY in urine (Table B.3.1.1.a) and for chlorpyrifos (CHLR) in dust (Table B.3.1.1.c) and solid food (Table B.3.1.1.g). This majority criterion will be described as "overall" in subsequent tables. Note that questions with spotty levels of significant relationships are not included in the type "c" table, although they are included in the type "a", and type "b" tables, and in the appendices.

It is important for the reader to review any results of interest with the details of the relationships, since information in the following tables is summarized across different studies and thus, across different populations, questionnaire instruments, and analytical measurement techniques. A starting point for this level of review is Appendix C, where the reader can examine both the defining situation and the results for individual relationships associated with a specific combination of questions, chemicals measured, and significance level.

Appendices B, C, and D include specific information about the relationships through overview, detail, and comment tables, respectively. The tables in each appendix are organized by question category, and then question within the category. A complete list of questions by category is included in Appendix E. The overview tables in Appendix B are a high level summary of the relationships found in the literature review, by question, medium, and chemical/metabolite measured. They provide a general indication of each question's effectiveness in identifying the exposure level to a specific chemical or metabolite. The detail tables in Appendix C present the specific statistical analysis and descriptive information for each relationship counted in that question category's overview table. Additional information about each relationship with respect to the subpopulation analyzed, the chemical measurement, and the statistical analysis are included in the comment tables in Appendix D. Instructions for reading these tables are included in each appendix. Information in both summary and detailed forms can be found for each question category as shown in Table 4.2.5.

Table 4.2.5 Cross-Reference for Relationship Tables by Question Category Group

Category			Section #	Table #[a]	Overview Table #	Detailed Table #	Comment Table #
Group	#	Description	Results	Results	Appendix B	Appendix C	Appendix D
Source	1	Residential pesticide use	4.2.4.1	4.2.6.x	B.3.1.1	C.3.1.1	D.3.1.1
Source	2	Household characteristics	4.2.4.2	4.2.7.x	B.3.1.2	C.3.1.2	D.3.1.2
Source	3	Residential sources (environmental measures)	4.2.4.3	4.2.8.x	B.3.1.3	C.3.1.3	D.3.1.3
Source	4	Household occupation	4.2.4.4	4.2.9.x	B.3.1.4	C.3.1.4	D.3.1.4
Source	5	Residential proximity to agricultural fields	4.2.4.5	4.2.10.x	B.3.1.5	C.3.1.5	D.3.1.5
Source	6	Residential location	4.2.4.6	4.2.11.x	B.3.1.6	C.3.1.6	D.3.1.6
Behavior	7	Subject's personal characteristics	4.2.5.1	4.2.13.x	B.3.2.1	C.3.2.1	D.3.2.1
Behavior	8	Child's behaviors	4.2.5.2	4.2.14.x	B.3.2.2	C.3.2.2	D.3.2.2
Behavior	9	Dietary behaviors	4.2.5.3	4.2.15.x	B.3.2.3	C.3.2.3	D.3.2.3
Behavior	10	Family hygiene practices	4.2.5.4	4.2.16.x	B.3.2.4	C.3.2.4	D.3.2.4
Behavior	11	Smoking-related activities	4.2.5.5	4.2.17.x	B.3.2.5	C.3.2.5	D.3.2.5
Behavior	12	Work exposure/practices	4.2.5.6	4.2.18.x	B.3.2.6	C.3.2.6	D.3.2.6
Other	13	Related exposure levels	4.2.6.1	4.2.20.x	B.3.3.1	C.3.3.1	D.3.3.1
Other	14	Health	4.2.6.2	4.2.21.x	B.3.3.2	C.3.3.2	D.3.3.2

[a] x in this column refers to the three table types, a, b, and c, described above.

The results for question categories under each of the three risk factors are presented in the following sections: source (section 4.2.4), behavior (section 4.2.5), and other (section 4.2.6).

Within each of these major sections, there is a subsection for each question category. Finally, a parallel construction of three summary table types (a, b, and c) is included for each question category.

4.2.4 Presentation of Source Relationships

Questions related to pesticide sources produced 387, or 64%, of the relationships found in this review (Table 4.2.3). The term "source" is used broadly here to include purposeful application of pesticides in the residential environment, measurements of pesticide levels in the residential environment, and incidental or accidental introduction of pesticides into the residential environment. The questions included in each of these categories can be found in Appendix E.

4.2.4.1 Category 1: Residential Pesticide Use

This category of questions (Appendix E) focuses on the purposeful application of pesticides in or around the residence, including indoor treatments for pests, outdoor treatments for insects, weeds, and other garden pests, and commercial applications of residential property.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category include: azinphosmethyl+phosmet, DAPs, and TCPY (Tables B.3.1.1.a-g); however, azinphosmethyl+phosmet did not have any significant relationships with questions from this category (Table B.3.1.1.c).

Table 4.2.6.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Residential Pesticide Use Category

Code(s)	Medium[a]	Description[b]
ATZ	other	Atrazine
CHLR	other	Chlorpyrifos
DAP2	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one detectable measurement)
DAP3	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one high measurement)[c]
ETHL1, ETHYL1	urine	DEP+DETP
ETHL3, ETHYL3	urine	DEP, DETP, DEDTP (at least one detectable measurement)
MDA	urine	Malathion dicarboxylic acid
MTHL2, METHYL2	urine	DMP+DMTP+DMDTP
MTHL3, METHYL3	urine	DMTP (detectable measurement)

Code(s)	Medium[a]	Description[b]
MTHL4, METHYL4	urine	DMP, DMTP (at least one detectable measurement)
TCPY	urine	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.
[c] See definition of high measurement in Azaroff (1999).

The residential pesticide use category includes 100 or 17% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions has the second highest occurrence of relationships. It is considered an important exposure source because children may be exposed during the application procedures, or may contact pesticide residues in the residential environment soon after application when residue levels can be relatively high.

Table 4.2.6.b Distribution of Significant Medium/Question Relationships for Residential Pesticide Use Questions, by Medium

	Medium/Question Relationships[a,b]			
	Significant[c]			
Medium Sampled	**Chemicals/Metabolites Measured[d]**	**N**	**%[e]**	**Total N**
Urine	MDA, TCPY, ETHYL1, ETHYL3, METHYL2, METHYL3, METHYL4, DAP2, DAP3	30	38	81
Dust	CHLR	1	13	8
Indoor air		0	0	2
Outdoor air		0	0	2
Personal air	ATZ, CHLR	3	75	4
Solid food	CHLR	1	33	3
Total		35	35	100

[a] See the paragraph immediately following Table 4.2.3, above, regarding relationships from Sexton (2003).
[b] Based on counts in Tables B.3.1.1.a through B.3.1.1.g.
[c] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[d] See descriptions in Table 4.2.6.a.
[e] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 81% of the relationships in this category (Tables B.3.1.1.a-g). This is much higher than the overall percentage of relationships with urine measurements (65.6%).

- The percent of relationships with dust measurements, 8%, is much lower than the overall percentage of 31% (Table B.3.1.1.c). This is not unexpected, since only a few of the studies for this category included dust sampling.
- TCPY and DAPs are the predominant metabolites measured in this category's urine-based relationships, 37% and 31%, respectively (Tables B.3.1.1.a-b).
- For TCPY, about 50% of the relationships are significant; for the DAPs, about 23% are significant (Table B.3.1.1.a). This difference may be due to the higher specificity of the TCPY metabolite; i.e., it is specific for chlorpyrifos or chlorpyrifos methyl, whereas the DAPs can be the result of multiple OP pesticides.
- Thirty-eight percent of the relationships with urine metabolites are significant or marginally significant (Table 4.2.10.b).
- Only one of the relationships with dust chemicals is significant (Table 4.2.10.b).

Relationships with other environmental measurements were found; however, they were found only in Sexton (2003) and the number of relationships was small (Tables B.3.1.1.d-g). The relationships were in the direction expected, that is, the activity was associated with higher exposure measurements.

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.6.c Residential Pesticide Use Questions and Chemicals/Metabolites with Overall[a] Significant Relationships[b]

Q#	Description	Medium	Chemicals/Metabolites Analyzed[c]
Q102	Inside Treated	Personal Air	CHLR
Q104	Inside Treated - Bedroom	Urine	TCPY
Q106	Inside Treated - Closets	Urine	TCPY
Q108	Inside Treated – Dining Room	Urine	TCPY
Q111	Inside Treated – Living Room	Urine	TCPY
Q117	Inside Treated – Other Room	Urine	TCPY
Q119	Outside Treated	Urine	MDA, TCPY
		Dust	CHLR
		Solid Food	CHLR
Q120	Garden Treated	Urine	TCPY, ETHYL1, METHYL2
Q121	Lawn/yard Treated	Urine	TCPY
Q124	Level of Pesticide Use	Urine	MDA, TCPY
		Personal Air	ATZ
Q125	Frequency Personal Application Inside	Urine	TCPY
Q126	Frequency Personal Application Outside	Urine	TCPY
Q127	Inside/Outside Treated by Family Member	Urine	ETHYL3, METHYL3, METHYL4, DAP2, DAP3
Q130	Personally Mixed Pesticide Inside	Urine	TCPY

[a] Overall indicates that > 50% of the question/medium/chemical relationships are significant.

[b] See the paragraph immediately following Table 4.2.3, above, regarding relationships from Sexton (2003).
[c] See descriptions in Table 4.2.6.a.

In most instances, and where information regarding the direction of the relationships is provided, the significant or marginally significant medium/question relationships are in agreement with the expectation that the exposure or activity is associated with a higher measurement level (Table C.3.1.1). Many of the significant relationships in Sexton (2003) (e.g., ID#s 562 and 567) show an effect opposite of what is expected. The publication speculated that the unexpected direction occurs either due to chance given the large number of relationships tested and/or in instances having a large number of non-detects. Note that questions regarding room-specific treatment are only available from Krinsley (1998) where the majority of respondents are adults. Overall the questions selected from this category (Table 4.2.6.c) appear to be useful predictors of exposure level for the chemicals and metabolites noted.

4.2.4.2 Category 2: Household Characteristics

Questions in this category (Appendix E) focus on unusual circumstances related to the household characteristics that might be associated with pesticide exposure. In particular, if property was used as a farm, there was a presumption that pesticide use might be greater or different than for other residences. Also, the movement of pets in and out of the house might lead to the track-in of pesticides that would not occur otherwise.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category include: azinphosmethyl, DAPs, a sum of selected OP pesticides, and TCPY (Tables B.3.1.2.a-d).

Table 4.2.7.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Household Characteristics Category

Code(s)	Medium[a]	Description[b]
AZM	other	Azinphosmethyl
CHLR	other	Chlorpyrifos
ETHL1, ETHYL1	urine	DEP+DETP
MDA	urine	Malathion dicarboxylic acid
MTHL2, METHYL2	urine	DMP+DMTP+DMDTP
OPSUM	other	OP Sum

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate;
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate
OP Sum = azinphosmethyl, chlorpyrifos, malathion, and phosmet.

The household characteristics category of questions includes 73 or 12% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the mid-range occurrence level of relationships. It is considered an important exposure source because young children spend a majority of their time in this environment -- their residence. Further the pesticide does not degrade as quickly indoors as it does outdoors, because there is less sunshine and air circulation indoors.

Table 4.2.7.b Distribution of Significant Medium/Question Relationships with Household Characteristics Questions, by Medium

	Medium/Question Relationships[a,b]			
	Significant[c]			Total
Medium Sampled	**Chemicals/Metabolites Measured[d]**	**N**	**%[e]**	**N**
Urine	ETHYL1,MDA, METHYL2	4	7	54
Dust	AZM, CHLR, OPSUM	3	17	18
Indoor air	CHLR	1	100	1
Total		8	11	73

[a] See the paragraph immediately following Table 4.2.3, above, regarding relationships from Sexton (2003).
[b] Based on counts in Tables B.3.1.2.a through B.3.1.2.d.
[c] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[d] See descriptions in Table 4.2.7.a.
[e] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 74% of the relationships in this category (Tables B.3.1.2.a-b). This is slightly higher than the overall percentage of relationships with urine measurements (65.6%).
- The percent of relationships with dust measurements, 25%, is slightly lower than the overall percentage of 31% (Table B.3.1.2.c).
- TCPY and DAPs are the predominant metabolites measured in this category's urine-based relationships (Tables B.3.1.2.a-b). Fifty percent of these relationships are with ethylated DAPs, and 31% are with methylated DAPs. This difference may be due to the higher specificity of the TCPY metabolite; i.e., it is specific for chlorpyrifos or chlorpyrifos methyl, whereas the DAPs can be the result of multiple OP pesticides.
- Seven percent of all the relationships with urine metabolites are significant (Table 4.2.7.b).
- Seventeen percent of the relationships with dust chemicals, and the one relationship with the indoor air chemical are significant (Table 4.2.7.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.7.c Household Characteristics Questions and Chemicals/Metabolites with Overall[a] Significant Relationships[b]

Q#	Description	Medium	Metabolites Analyzed[c]
Q202	Property Used As a Farm	Dust	CHLR
		Indoor Air	CHLR
Q209	Pets Inside/Outside House	Urine	MDA
Q211	Existence of Garden or Vegetable Garden	Urine	ETHYL1, MDA
Q213	Size of Household	Dust	AZM

[a] Overall indicates that > 50% of the question/medium/chemical relationships are significant.
[b] See the paragraph immediately following Table 4.2.3, above, regarding relationships from Sexton (2003).
[c] See descriptions in Table 4.2.7.a.

In most instances, and where information regarding the direction of the relationships is provided, the significant or marginally significant medium/question relationships are in agreement with the expectation that the exposure or activity is associated with a higher measurement level (Table C.3.1.2). Q202 includes only two relationships from Sexton (2003), and although they are significant and marginally significant, the relationships are in the opposite direction from what is expected. For example, property used as a farm would be expected to have higher measurement levels because of additional uses of pesticides; however, the levels in dust and indoor air were lower for farm property. The publication speculated that the unexpected direction occurred either due to chance given the large number of relationships tested and/or in instances having a large number of non-detects. Thus, the question may not be a useful predictor of a child's exposure level. The other questions selected from this category (Table 4.2.7.c) appear to be useful in predicting exposure level for the chemical or metabolite noted.

4.2.4.3 Category 3: Residential Sources (Environmental Measures)

This category of questions (Appendix E) focused on relationships between measurements of pesticides in the soil of residential environments and pesticides in house dust, as well as between measurements of pesticides in house dust and/or soil and pesticide metabolite levels in urine. In these cases the source of the pesticides in the environment was not known. Pesticide contamination could have occurred for any number of reasons. While the specific reason was not known in most cases, there was clear evidence that pesticides were present in the residential environment.

The chemicals/metabolites measured in the study samples are azinphosmethyl, chlorpyrifos, DAPs, ethyl parathion, and phosmet (Tables B.3.1.3.a-b).

Table 4.2.8.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Residential Sources Category

Code(s)	Medium[a]	Description[b]
AZM	other	Azinphosmethyl
CHLR	other	Chlorpyrifos
EPAR	other	Ethyl parathion
MTHL2, METHYL2	urine	DMP+DMTP+DMDTP
NA	urine	Not available in publication
PHSM	urine	Phosmet

[a] Medium is noted as urine or other (any other medium sampled)
[b] DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate

The residential source category of questions includes 13 or 2% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level of relationships. Relatively few of the studies under review collected house dust and urine samples concurrently and only Simcox (1995) collected soil and house dust samples concurrently. The very low pesticide concentrations found in soil in this study led later investigators to focus on house dust and other sources rather than soil.

Table 4.2.8.b Distribution of Significant Medium/Question Relationships with Residential Sources Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[a]			Total
Medium Sampled	Chemicals/Metabolites Measured[c]	N	% [d]	N
Urine	METHYL2, NA	4	80	5
Dust	AZM, CHLR, EPAR, PHSM	5	63	8
Total		9	69	13

[a] Based on counts in Tables B.3.1.3.a and B.3.1.3.b.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.8.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships in this category were found only between urine or dust sample concentrations and other environmental measurements (Tables B.3.1.3.a-b).
- The relationships with urine sample concentrations account for 38% of the relationships in this category (Table B.3.1.3.a). This is much lower than the overall percentage of relationships with urine measurements (65.6%).
- The percent of relationships with dust measurements, 62%, is much higher than the overall percentage of 31% (Table B.3.1.3.b). The higher percent of relationships with

dust as compared to urine is likely due to the role of house dust as a reservoir for pesticides in the home, whereas metabolite measurements reflect only exposure that may have occurred in the last 1-3 days.

- Eighty percent of the relationships with urine metabolites are significant (Table 4.2.8.b).
- Sixty-three percent of the relationships with dust chemicals are significant (Table 4.2.8.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.8.c Residential Sources Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed[b]
Q301	Household Dust	Urine	METHYL2, NA
Q303	Outdoor Soil	Dust	EPAR

[a] Overall indicates that > 50% of the question/medium/chemical relationships are significant.
[b] See descriptions in Table 4.2.8.a.

The relationships in this question category compared measurements, environmental to environmental, or environmental to urinary, and the statistical analyses used were correlations or regression analysis (Table C.3.1.3). When the direction of the relationships was provided for the significant or marginally significant relationships, the measurements generally increased together as expected. Thus, house dust and soil measurements (Table 4.2.8.c) may be considered useful in predicting exposure level.

4.2.4.4 Category 4: Household Occupation

Children who live in households where one or more of the adults has occupational exposures to pesticides may be at risk for increased exposure. This para-occupational exposure has been well demonstrated in studies of lead battery workers, asbestos workers, and others. A number of studies have been conducted recently to examine the extent to which pesticides used in the workplace are found in the home and whether this exposure pathway contributes to the body burden of children living in those homes. A list of the questions included in this category can be found in Appendix E.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category include: azinphosmethyl, chlorpyrifos, DAPs, ethyl parathion, and phosmet (Tables B.3.1.4.a-d).

Table 4.2.9.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Household Occupation Category

Code(s)	Medium[a]	Description[b]
AZM	other	Azinphosmethyl
AZMPH	other	Azinphosmethyl+Phosmet
CHLR	other	Chlorpyrifos
DAP2	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one detectable measurement)
DAP3	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one high measurement)[c]
DMTP	urine	Dimethylthiophosphate (DMTP)
EPAR	other	Ethyl parathion
ETHL3, ETHYL3	urine	DEP, DETP, DEDTP (at least one detectable measurement)
MTHL1, METHYL1	urine	DMTP+DMDTP
MTHL3, METHYL3	urine	DMTP (detectable measurement)
MTHL4, METHYL4	urine	DMP, DMTP (at least one detectable measurement)
MTHL5, METHYL5	urine	DMP, DMTP (at least one high measurement)[c]
OPSUM	other	OP Sum
PHSM	other	Phosmet

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate
OP Sum = azinphosmethyl, chlorpyrifos, malathion, and phosmet.
[c] See definition of high measurement in Azaroff (1999).

The household occupation category of questions includes 115 or 19% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions has the highest level of relationship occurrence. The pesticides used in agricultural workplaces can normally be identified with a high degree of specificity and the presence of these compounds in the home environment is clear evidence of workplace-to-residence chemical transmission.

Table 4.2.9.b Distribution of Significant Medium/Question Relationships with Household Occupation Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	Chemicals/Metabolites Measured[c]	N	%[d]	N
Urine	DAP2, DAP3, DMTP, ETHYL3, METHYL1, METHYL3, METHYL4, METHYL5	19	40	48
Dust	AZM, AZMPH, CHLR, EPAR, OPSUM, PHSM	28	47	59
Soil	AZM	1	13	8
Total		48	42	115

[a] Based on counts in Tables B.3.1.4.a through B.3.1.4.d.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.9.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 42% of the relationships in this category (Tables B.3.1.4.a-b). This is much lower than the overall percentage of relationships with urine measurements (65.6%).
- The percent of relationships with dust measurements, 51%, is much higher than the overall percentage of 31% (Table B.2.1.4.c). Dust is a convenient and stable medium for assaying the presence of agricultural chemicals in the home.
- Ethylated and methylated DAPs are the predominant metabolites measured in this category's urine-based relationships, 23% and 56%, respectively (Tables B.3.1.4.a-b).
- For ethylated DAPs, 18% of the relationships are significant (Table B.3.1.4.a-b).
- For methylated DAPs, 48% of the relationships are significant (Table B.3.1.4.a-b).
- Forty percent of the relationships with urine metabolites are significant or marginally significant (Table 4.2.9.b).
- Azinphosmethyl, chlorpyrifos, ethyl parathion, and phosmet are the predominant chemicals measured in this category's dust-based measurements. The percent of significant relationships for these chemicals is 42, 43, 56, and 8, respectively (Table B.3.1.4.c).
- Overall 47% of the relationships with dust chemicals are significant, and one relationship (13%) with a soil chemical is significant (Table 4.2.9.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.9.c Household Occupation Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed[b]
Q401	Agricultural Workers in Household	Dust	AZM
Q402	Household Member Spraying Fields	Urine	DAP2, DAP3, ETHYL3, METHYL3, METHYL4, METHYL5
Q403	Recent Fieldwork	Urine	DAP2, DAP3, METHYL4, METHYL5
Q404	Applicator vs Farmworker	Dust	AZMPH, EPAR
Q405	Applicator vs Non-applicator	Dust	CHLR, EPAR
Q406	Applicator vs Reference	Urine	DMTP
Q407	Applicator and Farmworker vs Reference	Urine	DMTP, METHYL1
		Dust	AZM, AZMPH, CHLR, EPAR, PHSM
Q409	Farmer and Farmworker vs Reference	Soil	AZM
Q412	Fieldworker vs Pesticide Handler	Dust	AZM
Q415	Tree Thinning	Dust	OPSUM
Q416	Number in household with high pesticide contact	Dust	OPSUM

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.9.a.

Based on the available information, the significant or marginally significant medium/question relationships seem to be in agreement with the expectation that the exposure or activity is associated with a higher measurement level (Table C.3.1.4). In some instances, no information regarding the direction of the relationships was provided. Questions under the Family Hygiene Practices and Work Practices/Exposures categories are also related to this exposure pathway. Overall, the questions selected in this category (Table 4.2.9.c) appear to be useful in predicting pesticide exposure levels.

4.2.4.5 Category 5: Residential Proximity to Agricultural Fields

Pesticide spray application remains a concern for families in agricultural communities and may contribute to a child's exposure. This is of particular concern as new housing developments are situated adjacent to working farms and where agricultural workers are housed, within or on the boundaries of agricultural fields. The distance between the residence and agricultural fields has been used as a surrogate metric for home contamination that can result from pesticide application spraying events. The accuracy of this metric is open to question, particularly when it is self-reported. More advanced methods of characterizing the link between agricultural pesticide use and human exposure are a topic of current scientific inquiry. A list of the questions included in this category can be found in Appendix E.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category include: azinphosmethyl, chlorpyrifos, ethyl parathion, and phosmet (Tables B.3.1.5.a-b).

Table 4.2.10.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Residential Proximity to Agricultural Fields Category

Code(s)	Medium[a]	Description[b]
AZM	other	Azinphosmethyl
AZMPH	other	Azinphosmethyl+Phosmet
CHLR	other	Chlorpyrifos
DMTP	urine	Dimethylthiophosphate (DMTP)
EPAR	other	Ethyl parathion
MTHL1, METHYL1	urine	DMTP+DMDTP

[a] Medium is noted as urine or other (any other medium sampled).
[b] DMP = dimethylphosphate, DMTP = dimethylthiophosphate.

The residential proximity to agricultural fields category of questions includes 72 or 12% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the mid-range occurrence level of relationships. The possibility of misclassification of exposure potential through use of a simple residential proximity metric is relatively high. In most cases, it is not known when, or even if, the nearby fields were treated with pesticides nor is it known what compounds may have been used. Factors, such as wind direction and application procedures, are important variables that are not accounted for in the use of residential proximity.

Table 4.2.10.b Distribution of Significant Medium/Question Relationships with Residential Proximity to Agricultural Fields Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	Chemicals/Metabolites Measured[c]	N	%[d]	N
Urine	DMTP, METHYL1	4	13	30
Dust	AZM, AZMPH, CHLR, EPAR	16	38	42
Total		20	28	72

[a] Based on counts in Tables B.3.1.5.a and B.3.1.5.b.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.10.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 42% of the relationships in this category (Table B.3.1.5.a). This is much lower than the overall percentage of relationships with urine measurements (65.6%).
- The percent of relationships with dust measurements, 58%, is much higher than the overall percentage of 31% (Table B.3.1.5.b). Dust is a convenient and stable medium for attempting to track the impact of agricultural pesticide use on residential environments.
- Methylated DAPs are the predominant metabolites measured (67%) in this category's urine-based relationships, but only 20% of those relationships are significant (Table B.3.1.5.a). Many of the studies that have explored this relationship have been conducted in agricultural regions where methyl DAPs are used for insect control.
- Thirteen percent of the relationships with urine metabolites are significant (Table 4.2.10.b).
- Azinphosmethyl, chlorpyrifos, ethyl parathion, and phosmet are the predominant chemicals measured in this category's dust-based measurements. The percent of significant relationships for these chemicals is 31, 38, 56, and 0, respectively (Table B.3.1.5.b).
- Overall 38% of the relationships with dust chemicals are significant (Table 4.2.10.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.10.c Residential Proximity to Agricultural Fields Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed[b]
Q501	Proximity of Home to Pesticide-Treated Farmland/Orchard	Urine	DMTP
		Dust	AZMPH, EPAR

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.10.a

In most instances, the significant or marginally significant media/question relationships are in agreement with the expectation that the exposure or activity is associated with a higher measurement level (Table C.3.1.5). In some instances, no information regarding the direction of the relationships is provided. Thus, proximity of the home to pesticide-treated farmland or orchards appears to be useful for predicting exposure for the chemicals and metabolites noted (Table 4.2.10.c).

4.2.4.6 Category 6: Residential Location

This category of questions (Appendix E) was developed to capture aspects of residential location other than proximity to agricultural fields. In particular, some studies have compared urban and rural residential environments on the assumption that rural environments might provide a greater opportunity for children's exposure to pesticides. Also, some studies have examined the relationship between pesticide concentrations in house dust and vehicle dust, based on the theory that the vehicle may serve as a vector for pesticide transmission into the home and as a direct source of exposure when children are transported.

The chemicals/metabolites measured in the study samples are 1-naphthol, malathion dicarboxylic acid, TCPY, ethylated DAPs, and azinphosmethyl (Tables B.3.1.6.a-b); however, only azinphosmethyl and TCPY had any significant relationships.

Table 4.2.11.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Residential Location Category

Code(s)	Medium[a]	Description
AZM	other	Azinphosmethyl
TCPY	urine	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled)

The residential location category of questions includes 14 or 2% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level of relationships. Only a few studies have examined these relationships, so data for this category is limited.

Table 4.2.11.b Distribution of Significant Medium/Question Relationships with Residential Location Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	**Chemicals/Metabolites Measured[c]**	**N**	**%[d]**	**N**
Urine	TCPY	3	23	13
Dust	AZM	1	100	1
Total		4	29	14

[a] Based on counts in Tables B.3.1.6.a and B.3.1.6.b.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.11.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 93% of the relationships in this category (Table B.3.1.6.a). This is much higher than the overall percentage of relationships with urine measurements (65.6%). Most studies that have explored these relationships have focused on urinary metabolite measurements.

- There is only one relationship with a dust sample concentration (Table B.3.1.6.b). Studies of this kind have not been conducted frequently. They focus on worker commuter vehicles as part of an exposure pathway for children, and this has only recently been recognized as a potential contributor to exposure.
- TCPY is the predominant metabolite measured (36%) in this category's urine-based relationships, but only 3 (60%) of its relationships are significant (Table B.3.1.6.a). It is not surprising to find that the relationships between questions and TCPY metabolites were not found to be significant. Chlorpyrifos, the parent compound of the TCPY metabolite, has been until recently the most widely used OP pesticide in the United States. Furthermore, diet is an important source of chlorpyrifos exposure, so a simple categorization of homes as urban or rural would be unlikely to demonstrate differential body burdens in children.
- Overall, 23% of the relationships with urine metabolites are significant (Table 4.2.11.b)
- The one relationship with azinphosmethyl in dust is also significant (Table 4.2.11.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.11.c Residential Location Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed[b]
Q601	Urban vs Non-urban	Urine	TCPY
Q605	Vehicle vs House	Dust	AZM

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.11.a.

In most instances where information regarding the direction of the relationships is provided, the significant or marginally significant media/question relationships were in agreement with the expectation that the exposure or activity would be associated with a higher measurement level (Table C. 3.1.6). Thus, although the number of relationships evaluated for questions in this category is small, the questions selected (Table 4.2.11.c) appear to be useful in predicting exposure level for the chemical and metabolite noted.

4.2.4.7 Summary of Results from Source Relationships

The six question categories under the source risk factor represent sources of exposure in the residential environment. Thirty-five questions from these categories are considered overall statistically significant (and effective differentiators of pesticide exposure levels) for the chemicals/metabolites noted (Table 4.2.12). For each of the question and chemical/metabolite combinations, the majority (> 50%) of the relationships were statistically or marginally significant.

Table 4.2.12 Questions from Source Categories Considered Overall Statistically Significant, by Medium

Medium	Q Category	Q #[a]	Q Description	Chemicals/ Metabolites[b]
Dust				
	Residential pesticide use	Q119	Outside Treated[c]	CHLR
	Household characteristics	Q202	Property Used As a Farm[c]	CHLR
	Residential environment (environmental measures)	Q213	Size of Household	AZM
	Residential sources	Q303	Outdoor Soil	EPAR
	Household occupation	Q401	Agricultural Workers in Household	AZM
		Q404	Applicator vs Farmworker	AZMPH, EPAR
		Q405	Applicator vs Non-applicator	CHLR, EPAR
		Q407	Applicator and Farm worker vs Reference	AZM, AZMPH, CHLR, EPAR, PHSM
		Q412	Fieldworker vs Pesticide Handler	AZM
		Q415	Tree Thinning	OPSUM
		Q416	Number in Household with High Pesticide Contact	OPSUM
	Residential proximity to agricultural fields	Q501	Proximity of Home to Pesticide-Treated Farmland/Orchard	AZMPH, EPAR
	Residential location	Q605	Vehicle vs House	AZM
Indoor Air				
	Household characteristics	Q202	Property Used As a Farm[c]	CHLR
Personal Air				
	Residential pesticide use	Q102	Inside Treated	CHLR
		Q124	Level of Pesticide Use[c]	ATZ
Soil				
	Household occupation	Q409	Farmer and Farm worker vs Reference	AZM
Solid Food				
	Residential pesticide use	Q119	Outside Treated[c]	CHLR
Urine				
	Residential pesticide use	Q104	Inside Treated - Bedroom	TCPY
		Q106	Inside Treated - Closets	TCPY
		Q108	Inside Treated – Dining Room	TCPY

Medium	Q Category	Q #[a]	Q Description	Chemicals/ Metabolites[b]
		Q111	Inside Treated -- Living Room	TCPY
		Q117	Inside Treated -- Other Room	TCPY
		Q119	Outside Treated[c]	MDA, TCPY
		Q120	Garden Treated	TCPY, ETHYL1, METHYL2
		Q121	Lawn/Yard Treated[c]	TCPY
		Q124	Level of Pesticide Use[c]	MDA, TCPY
		Q125	Frequency Personal Application Inside	TCPY
		Q126	Frequency Personal Application Outside	TCPY
		Q127	Inside/Outside Treated by Family Member	ETHYL3, METHYL3, METHYL4, DAP2, DAP3
		Q130	Personally Mixed Pesticide Inside	TCPY
	Household characteristics	Q208	Pets in House	METHYL2
		Q209	Pets Inside/Outside House[c]	MDA
		Q211	Existence of Garden or Vegetable Garden[c]	ETHYL1, MDA
	Residential sources (environmental measures)	Q301	Household Dust	METHYL2, NA
	Household occupation	Q402	Household Member Spraying Fields	DAP2, DAP3, ETHYL3, METHYL3, METHYL4, METHYL5
		Q403	Recent Fieldwork	DAP2, DAP3, METHYL4, METHYL5
		Q406	Applicator vs Reference	DMTP
		Q407	Applicator and Farm worker vs Reference	DMTP, METHYL1
	Residential proximity to agricultural fields	Q501	Proximity of Home to Pesticide-Treated Farmland/Orchard	DMTP
	Residential location	Q601	Urban vs Non-urban	TCPY

[a] For some of the significant relationships, the effect of the exposure factor was not in the direction expected. See Appendix C for details on specific questions.
[b] Chemicals or metabolites for which > 50% of the relationships with the question were statistically or marginally significant. (See "a" tables: Tables 4.2.6.a through 4.2.11.a for descriptions.)
[c] See Section 4.2.2 regarding relationships from Sexton (2003).

Household occupation was a strong differentiator for pesticide levels in dust which relate to the take-home pathway exposure. Residential pesticide use and household occupation were strong differentiating categories for the urine metabolite levels (Table 4.2.12).

4.2.5 Presentation of Behavior Relationships

Many exposure studies include questions that focus on the behavior of household members or children. The temporal and spatial patterns of children's activities are important variables in exposure assessment, generally referred to as macro-activities. Additionally, activities conducted in specific microenvironments, such as crawling, contact with objects, hand-to-mouth behavior, and object-to-mouth behavior – generally referred to as micro-activities – are thought to contribute significantly to dermal, oral, and respiratory exposures among children. Behavior accounted for 203, or 34%, of observed relationships in this review (Table 4.2.3).

4.2.5.1 Category 7: Subject's Personal Characteristics

A number of studies have collected demographic information, such as age, gender, ethnicity, and income level, and have explored possible associations with pesticide metabolite levels in urine. These analyses have been undertaken in an effort to determine if there are consistent trends related to subject information that is often readily available through census or other databases. A list of the questions included in this category can be found in Appendix E.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category are DAPs (Tables B.3.2.1.a-b).

Table 4.2.13.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Subject's Personal Characteristics Category

Code(s)	Medium[a]	Description[b]
1NAP	urine	1-Naphthol
DAP1	urine	DMP+DMTP+DMDTP+DEP+DETP+DEDTP
DMTP	urine	Dimethylthiophsophate (DMTP)
ETHL2, ETHYL2	urine	DEP+DETP+DEDTP
MDA	urine	Malathion dicarboxylic acid
MTHL2, METHYL2	urine	DMP+DMTP+DMDTP
TCPY	urine	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.

The subject's personal characteristics category of questions includes 78 or 13% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the mid-range occurrence level of relationships. Information regarding age, gender, ethnicity and income is relatively easy to obtain, but, with the exception of age, it is not clear that these characteristics would be related to pesticide exposures.

Table 4.2.13.b Distribution of Significant Medium/Question Relationships with Subject's Personal Characteristics Questions, by Medium

Medium/Question Relationships[a]				
	Significant[b]			Total
Medium Sampled	Chemicals/Metabolites Measured[c]	N	%[d]	N
Urine	1NAP, DAP1, DMTP, ETHYL2, MDA, METHYL2, TCPY	22	28	78
Total		22	28	78

[a] Based on counts in Tables B.3.2.1.a and B.3.2.1.b.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.13.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine concentrations were found for this category (Tables B.3.2.1.a-b).
- Twenty-eight percent of the relationships are significant (Table 4.2.13.b).
- The percent of significant relationships for each metabolite is (Tables B.3.2.1.a-b):
    - Ethylated DAPs – 12%,
    - Methylated DAPs – 27%
    - Ethylated+methylated DAPs – 40%
    - 1-Naphthol – 50%
    - MDA – 67%
    - TCPY – 30%.

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.13.c Subject's Personal Characteristics Questions and Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Metabolites Analyzed[b]
Q702	Age	Urine	DAP1, METHYL2
Q703	Ethnicity	Urine	1NAP, MDA
Q705	Income	Urine	1NAP, MDA, TCPY

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.13.a.

Based on the significant relationships, younger children have higher levels of metabolites than older children, and children have higher levels than adults (Table C.3.2.1). Thus, age appears to be a useful predictor of pesticide exposure level in the metabolites noted (Table 4.2.13.c). The significant ethnic and income relationships found in Adgate (2001) were not consistently in the same direction, and given the small number of relationships found in the publications, they do not appear to be useful predictors of pesticide exposure levels.

4.2.5.2 Category 8: Child's Behaviors

This category includes children's behaviors, actions, and activities that may differentiate children's pesticide exposure levels. Factors include both habits and hygiene practices of children such as sucking thumbs and the frequency and timing of hand washing. Time related activities such as the amount of time children spend in certain environments (e.g. indoors, outdoors, or at school) can also contribute to measurable differences in their pesticide exposure levels. A limited number of studies have included children's hand wipes as an exposure metric and compared pesticide loading values with metabolite levels. A list of the questions included in this category can be found in Appendix E.

The metabolites measured in the study samples are 4-nitrophenol, DAPs, and TCPY (Table B.3.2.2.a); however, only the DAP metabolite has significant relationships with the questions in this category (Table 4.2.14.a).

Table 4.2.14.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Child's Behaviors Category

Code(s)	Medium[a]	Description[b]
DAP1	urine	DMP+DMTP+DMDTP+DEP+DETP+DEDTP

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.

The child's behaviors category of questions includes 20 or 3% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level of relationships. It is considered an important exposure factor, since most investigators believe that a child's behavior will have a significant impact on pesticide exposure (e.g., see Cohen Hubal (2000b), Black (2005), Reed (1999), Freeman (2005)).

Table 4.2.14.b Distribution of Significant Medium/Question Relationships with Child's Behaviors Questions, by Medium

Medium/Question Relationships[a]				
	Significant[b]			Total
Medium Sampled	Metabolites Measured[c]	N	% [d]	N
Urine	DAP1	2	10	20
Total		2	10	20

[a] Based on counts in Table B.3.2.2.a
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.14.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine-based relationships were found for this category (Table B.3.2.2.a).
- Ten percent of the relationships are significant or marginally significant (Table 4.2.14.b), and the significant relationships were with the DAP metabolite (Table B.3.2.2.a).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.14.c Child's Behaviors Questions and Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Metabolites Analyzed
Q806	Loading from hand wipe	Urine	DAP1

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.

No questions in this category have overall significant relationships with urine measurements (Table C.3.2.2); however, the loading measurement from the hand wipe (Table 4.2.14.c) does have a significant relationship. Overall, questions available in the category of child's behaviors do not appear to be useful in predicting the child's pesticide exposure level.

4.2.5.3 Category 9: Dietary Behaviors

Diet is likely to be a major pathway of pesticide exposure for most children, yet few studies have examined this issue directly. The U.S. EPA has made a substantial effort to develop quantitative estimates of dietary pesticide through the combination of food consumption surveys and analysis of pesticide residues in common food products. Nonetheless, there remains substantial uncertainty in the ability to predict an individual's pesticide ingestion based on food diaries or food frequency questionnaires. In this review, only one study was placed in this category. Additional studies are underway, and should add to the understanding of this pathway. A list of the questions included in this category can be found in Appendix E.

The metabolites measured in the study samples are DAPs and TCPY (Table B.3.2.3.a); however, only a DAP metabolite had significant relationships for this category.

Table 4.2.15.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Dietary Behaviors Category

Code(s)	Medium[a]	Description[b]
MTHL2, METHYL2	urine	DMP+DMTP+DMDTP

[a] Medium is noted as urine or other (any other medium sampled).
[b] DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.

The dietary behaviors category of questions includes 16 or 3% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level of relationships, which is due primarily to the lack of studies that have focused on this pathway.

Table 4.2.15.b Distribution of Significant Medium/Question Relationships with Dietary Behaviors Questions, by Medium

Medium/Question Relationships[a]				
	Significant[b]			Total
Medium Sampled	Metabolites Measured[c]	N	%[d]	N
Urine	METHYL2	2	13	16
Total		2	13	16

[a] Based on counts in Table B.3.2.3.a.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.15.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine-based relationships were found for this category (Table B.3.2.3.a).
- The significant relationships are for a methylated DAP sum (Table B.3.2.3.a), and account for 13% of the urine-based relationships (Table 4.2.15.b). A number of studies have found that the methyl DAPs are more common than ethyl DAPs in urine. See, for example, the most recent NHANES data (Barr 2004).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.15.c Dietary Behaviors Questions and Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Metabolites Analyzed[b]
Q904	Organic Diet	Urine	METHYL2

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.15.a

Based on the significant relationships, a conventional diet has higher pesticide metabolite levels than an organic diet (Table C.3.2.3). Although the number of relationships for this question is small, it appears to be useful in predicting methylated DAP metabolite levels.

4.2.5.4 Category 10: Family Hygiene Practices

Many investigators have placed an emphasis on good hygienic practices within the home as a means of reducing children's exposure to pesticides. For example, it is common for public health scientists and practitioners to recommend that agricultural workers remove their work boots before entering the home and that work clothing be washed separately from the family clothing. Thus, family hygiene is an important variable to investigate in studies of children's pesticide exposure. A list of the questions included in this category can be found in Appendix E.

The chemicals/metabolites measured in the study samples having the most medium/question relationships in this category include: azinphosmethyl, chlorpyrifos, dimethylthiophosphate (DMTP), and ethyl parathion (Tables B.3.2.4.a-b).

Table 4.2.16.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Family Hygiene Practices Category

Code(s)	Medium[a]	Description
AZM	other	Azinphosmethyl
DMTP	urine	Dimethylthiophosphate
OPSUM	other	OP Sum[b]

[a] Medium is noted as urine or other (any other medium sampled)
[b] OP Sum = azinphosmethyl, chlorpyrifos, malathion, and phosmet.

The family hygiene practices category of questions includes 81 or 13% of the relationships extracted from the relevant publications. This category of questions falls into the mid-range occurrence level of relationships (Table 4.2.3). Many of the studies under review have been conducted in agricultural communities, so it is not surprising that questions related to family hygiene would occur with some frequency.

Table 4.2.16.b Distribution of Significant Medium/Question Relationships with Family Hygiene Practices Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	**Chemicals/Metabolites Measured[c]**	**N**	**%[d]**	**N**
Urine	DMTP	2	6	33
Dust	AZM, OPSUM	3	6	48
Total		5	6	81

[a] Based on counts in Tables B.3.2.4.a and B.3.2.4.b.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.16.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 41% of the relationships in this category (Table B.3.2.4.a). This is much lower than the overall percentage of relationships with urine measurements (65.6%).
- The percent of relationships with dust measurements, 59%, is much higher than the overall percentage of 31% (Table B.3.2.4.b). Dust is used commonly as a metric for home contamination by workplace chemicals, since its measurement is more stable than urinary metabolites.
- DMTP is the predominant metabolite measured (48%) in this category's urine-based relationships (Table B.3.2.4.a).
- Only 6% of the relationships with DMTP are significant (Table 4.2.16.b), and these are the only urine-based relationships that are significant (Table B.3.2.4.a).
- For dust concentrations, azinphosmethyl, chlorpyrifos, and ethyl parathion were the predominant chemicals measured, 25%, 21%, and 21%, respectively (Table B.3.2.4.b).
- Overall, only six percent of the relationships with dust concentrations are significant (Table 4.2.16.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.16.c Family Hygiene Practices Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed[b]
Q1006	Work Clothes Worn Indoors	Dust	AZM, OPSUM
Q1009	Number of Weeks Since Last Vacuuming	Dust	OPSUM

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.16.a.

In instances where information regarding the direction of the relationships is provided, the significant or marginally significant media/question relationships are in agreement with the expectation that the exposure or activity is associated with a higher measurement level (Table C.3.2.4). Both longer periods of wearing work clothes indoors and more weeks since last vacuuming were associated with higher measurement levels of dust. Although there are a small number of relationships for these questions, they appear to be useful in predicting exposure levels in dust for the chemicals noted (Table 4.2.16.c).

4.2.5.5 Category 11: Smoking-Related Activities

Several studies have included the measurement of urinary cotinine, the primary metabolite of nicotine, as a marker of children's exposure to smoking. Smoking at the workplace has been associated with higher pesticide exposures since cigarettes or other smoking material may become contaminated during work. It is not clear, however, that there is a plausible hypothesis for an effect of adult smoking behavior on children's pesticide exposure. A list of the questions included in this category can be found in Appendix E.

The only chemical/metabolite measured in the study samples was TCPY (Table B.3.2.5.a).

Table 4.2.17.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Smoking-Related Activities Category

Code(s)	Medium[a]	Description
TCPY	urine	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled).

The smoking-related activities category of questions includes 4 or 1% of the relationships extracted from the relevant publications (Table 4.2.3) and falls into the low-range occurrence level. This finding is not surprising, since there would appear to be little relationship between smoking and pesticide metabolite levels in children.

Table 4.2.17.b Distribution of Significant Medium/Question Relationships with Smoking-Related Activities Questions, by Medium

	Medium/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	Metabolites Measured[c]	N	%[d]	N
Urine	TCPY	3	75	4
Total		3	75	4

[a] Based on counts from Table B.3.2.5.a.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.17.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine-based relationships were found for this category (Table B.3.2.5.a).
- Seventy-five percent of the relationships with TCPY are significant (Table 4.2.17.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.17.c Smoking-Related Activities Questions and Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Metabolites Analyzed[b]
Q1101	Current Smoker	Urine	TCPY
Q1102	Subject Smoked	Urine	TCPY

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.17.a.

The two questions in Table 4.2.17.c were from Krinsley (1998) whose study population was focused on adults, but included children greater than 10 years of age. For Q1102, the two relationships are significant; however, the direction of the relationship differs depending on the other questions included in the regression analysis. For Q1101, the direction of the effect is opposite of what is expected; that is, higher measurement levels are not associated with currently smoking. Thus, the relationship between smoking and TCPY levels in urine appears not to be supported by a plausible hypothesis (Table C.3.2.5).

4.2.5.6 Category 12: Work Exposure/Practices

Work exposure and work practices may lead to children's pesticide exposure if pesticides are transmitted from the workplace to the home. The studies under review were primarily environmental exposures studies conducted in agricultural communities with a focus on children. If these studies had been strictly occupational exposure assessment studies, more questions related to the work and family hygiene practices might have been included in these studies. A list of the questions included in this category can be found in Appendix E.

The chemicals/metabolites measured in the study samples are azinphospmethyl and TCPY (Table B.3.2.6.a); however, none of the chemicals/metabolites have significant relationships with questions in this category (Table 4.2.18.a).

Table 4.2.18.a Codes and Descriptions for Chemicals/Metabolites with Significant Relationships for Questions in the Work Exposure/Practices Category

Code(s)	Medium	Description
None	urine, dust	No chemicals

The work exposure/practices category of questions includes 4 or 1% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level of relationships.

Table 4.2.18.b Distribution of Significant Relationships with Work Exposure/Practices Questions, by Medium

	Media/Question Relationships[a]			
	Significant[b]			Total
Medium Sampled	**Chemicals/Metabolites Measured[c]**	**N**	**%[d]**	**N**
Urine	None	0	0	1
Dust	None	0	0	3
Total		0	0	4

[a] Based on counts in Table B.3.2.6.a.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.18.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Relationships between questions and urine sample concentrations account for 25% of the relationships in this category (Table B.3.2.6.a).
- Seventy-five percent of the relationships are dust-based (Table B.3.2.6.b).
- None of the relationships with urine metabolites or dust chemicals are significant or marginally significant (Table 4.2.18.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.18.c Work Exposure/Practices Questions and Chemicals/Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Chemicals/Metabolites Analyzed
N/A	Not applicable	Urine, dust	Not applicable

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.

No questions (Table 4.2.18.c) in this category have significant relationships with the urine and dust measurements (Table C.3.2.6) for the studies considered in this review.

4.2.5.7 Summary of Results from Behavior Relationships

The six question categories under the behavior risk factor focus on the behaviors of the household members or children in both macro and micro environments. Nine questions from five of the six question categories are considered overall statistically significant (and effective differentiators of exposure level) for the chemicals/metabolites noted. For each of the question and chemical/metabolite combinations, the majority (> 50%) of the relationships were statistically or marginally significant.

Table 4.2.19 Questions from Behavior Question Categories Considered Overall Statistically Significant, by Medium

Medium	Q Category	Q #[a]	Q Description	Chemicals/ Metabolites[b]
Dust				
	Family hygiene practices	Q1006	Work Clothes Worn Indoors	AZM, OPSUM
		Q1009	Number of Weeks Since Last Vacuuming	OPSUM
Urine				
	Subject's personal characteristics	Q702	Age	DAP1, METHYL2
		Q703	Ethnicity	1NAP, MDA
		Q705	Income	1NAP, MDA, TCPY, DMTP, DAP1
	Child's behaviors	Q806	Loading from Hand Wipe	DAP1
	Dietary behaviors	Q904	Organic Diet	METHYL2
	Smoking-related activities	Q1101	Current Smoker[c]	TCPY
		Q1102	Subject Smoked[c]	TCPY

[a] For some of the significant relationships, the effect of the exposure factor was not in the direction expected. See Appendix C for details on specific questions.
[b] Chemicals or metabolites for which > 50% of the relationships with the question were statistically or marginally significant. (See "a" tables: Tables 4.2.13.a through 4.2.18.a for descriptions.)
[c] Included only in Krinsley (1998) whose study population was focused on adults, but included children greater than 10 years of age.

Family hygiene practices were the strong differentiators for pesticide levels in dust measurements; the subject's personal characteristics, the child's behaviors, and dietary behaviors were the strong differentiators for the pesticide metabolite levels in urine (Table 4.2.19).

4.2.6 Presentation of Other Relationships

Several other relationships were tested in the studies under review, but these were difficult to categorize. Two types of relationships are discussed here: exposure levels in populations (in particular, in adults living with children), and health outcomes. This category included 13, or 2%, of the relationships identified in this review.

4.2.6.1 Category 13: Related Exposure Levels

Several studies examined the relationship between pesticide metabolite levels in adults and children. It was hypothesized in these studies that adults living in the same environment as children, and perhaps consuming similar foods, would exhibit similar metabolite levels. A list of the questions included in this category can be found in Appendix E.

Table 4.2.20.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Related Exposure Levels Category

Code(s)	Medium[a]	Description[b]
DAP2	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one detectable measurement)
DAP3	urine	DEP, DETP, DEDTP, DMP, DMTP (at least one high measurement)[c]
MTHL4, METHYL4	urine	DMP, DMTP (at least one detectable measurement)

[a] Medium is noted as urine or other (any other medium sampled).
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate
[c] See definition of high measurement in Azaroff (1999).

The related exposure levels category of questions includes 5 or 1% of the relationships extracted from the relevant publications. This category of questions falls into the low-range occurrence level for relationships (Table 4.2.3). An association between adult and child pesticide metabolite levels suggests similar exposure sources for these populations, and may help in understanding how to reduce or prevent exposures. However, few studies have examined this relationship.

Table 4.2.20.b Distribution of Significant Relationships with Related Exposure Levels Questions, by Medium

	Media/Question Relationships[a]			
Medium Sampled	Significant[b]			Total
	Metabolites Measured[c]	N	%[d]	N
Urine	DAP2, DAP3, METHYL4	4	80	5
Total		4	80	5

[a] Based on counts in Table B.3.3.1.a.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.20.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine-based relationships were found for this category (Table B.3.3.1.a).

- Eighty percent of the relationships are significant (Table 4.2.20.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.20.c Related Exposure Levels Questions and Metabolites with Overall[a] Significant Relationships

Q#	Description	Medium	Metabolites Analyzed[b]
Q1302	High Levels in Adult Household Members	Urine	DAP2, DAP3, METHYL4

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.20.a

In most instances where information regarding the direction of the relationships is provided, the significant medium/question relationships are in agreement with the expectation that more adults in the household with high measurement levels is associated with a higher measurement level for the children (Table C.3.3.1). Although there are a small number of relationships for this question, it appears to be a useful predictor of DAP levels in urine.

4.2.6.2 Category 14: Health

In some of the studies under review investigators included general health status questionnaires. It is not clear whether such questions were included to collect general health status information on the population, or to explore specific hypotheses related to pesticide exposure. For example, it is not immediately evident why pesticide exposure would be associated with intestinal disease or ulcers, unless one considers a possible change in diet to be associated with such diseases. Nevertheless, possible associations between health outcomes and pesticide exposure metrics were tested in some instances. A list of the questions included in this category can be found in Appendix E.

The only metabolite measured in the study samples for this category is TCPY (Table B.3.3.2.a).

Table 4.2.21.a Codes and Descriptions for Metabolites with Significant Relationships for Questions in the Health Category

Code(s)	Medium[a]	Description
TCPY	urine	3,5,6-Trichloro-2-pyridinol

[a] Medium is noted as urine or other (any other medium sampled).

The health category of questions includes 8 or 1% of the relationships extracted from the relevant publications (Table 4.2.3). This category of questions falls into the low-range occurrence level. The possible association of TCPY metabolites in urine with health outcomes does not imply causality in either direction. Associations that do not involve the nervous system are generally not supported by a well-established hypothesis; however, the OP pesticides may affect the nervous system such that other organ systems can also be affected. Analyses of these types of possible associations should be considered exploratory.

Table 4.2.21.b Distribution of Significant Relationships with Health Questions, by Medium

	Media/Question Relationships[a]			
Medium Sampled	Significant[b]			Total
	Chemicals/Metabolites Measured[c]	N	%[d]	N
Urine	TCPY	5	63	8
Total		5	63	8

[a] Based on counts in Table B.3.3.2.a.
[b] Significant ($p < 0.05$) and marginally significant ($p < 0.10$).
[c] See descriptions in Table 4.2.21.a.
[d] Percent of significant relationships for medium, that is, (N*100)/Total N.

The relationships in this question category can be summarized as follows:

- Only urine-based relationships were found for this category (Table B.3.3.2.a).
- Sixty-three percent of the relationships with TCPY are significant (Table 4.2.21.b).

See Table 4.2.5 for tables with related information for the questions in this category.

Table 4.2.21.c Health Questions and Metabolites with Overall[a] Significant Relationships

	Description	Medium	Metabolites Analyzed[b]
Q1403	Bowel Disease	Urine	TCPY
Q1405	Intestinal Disease	Urine	TCPY
Q1406	Ulcers	Urine	TCPY

[a] Overall indicates that > 50% of the question/medium/chemical relationships were significant.
[b] See descriptions in Table 4.2.21.a

In most of the significant relationships, not having the disease is associated with a higher TCPY level than having the disease; however several of these analyses included the question as one of several in a regression analysis, and the direction of the relationship cannot be determined by the regression coefficient alone (Table C.3.3.2). These relationships did not necessarily consider the health outcome of pesticide exposure; however, it is possible that health status may signal changes in dietary or other behaviors that may affect exposure levels. One example is the inclusion or exclusion of additional vegetables and fruits in the diet.

4.2.6.3 Summary of Results from Other Relationships

The two question categories under the "other" risk factor were difficult to categorize. Four questions from the two question categories are considered overall statistically significant (and effective differentiators of pesticide exposure levels) for TCPY. For each of the question and chemical/metabolite combinations, the majority (> 50%) of the relationships were statistically or marginally significant.

Table 4.2.22 Questions from Other Question Categories Considered Overall Statistically Significant, by Medium

Medium	Q Category	Q #[a]	Q Description	Chemicals/ Metabolites[b]
Urine				
	Related exposure levels	Q1302	High Levels in Adult Household Members	DAP2, DAP3, METHYL4
	Health	Q1403	Bowel Disease	TCPY
		Q1405	Intestinal Disease	TCPY
		Q1406	Ulcers	TCPY

[a] For some of the significant relationships, the effect of the exposure factor was not in the direction expected. See Appendix C for details on specific questions.
[b] Chemicals or metabolites for which > 50% of the relationships with the question were statistically or marginally significant. (See "a" tables: Tables 4.2.21.a and 4.2.22.a for descriptions.)

Neither of the question categories showed differentiating capability for pesticide levels in dust measurement levels (Table 4.2.22). Both categories have some questions that differentiate pesticide metabolite levels in urine.

4.2.7 Summary of Results from Literature Review

Tables 4.2.12, 4.2.19, and 4.2.22 list the questions that are strong differentiators for the chemical or metabolite levels for each of the three risk factors, source, behavior, and other. Dust and urine measurements were found in 97% of the relationships. Measurements for the other media were found in only two of the 20 publications: Sexton (2003) and Simcox (1995). The relationships for each question and chemical/metabolite combination were reviewed to determine the question's effectiveness for differentiating the exposure levels. Not all question/chemical combinations were evaluated in the studies to the same extent. The number of relationships evaluated with a question, especially when the questions are used with more than one study population, gives additional credence to the question as a potential differentiator for a specific chemical or metabolite. Generally the questions showing the most effectiveness were:

- residential pesticide use (inside and outside)
- occupation of household members
- child's characteristics (age, ethnicity, income)
- family hygiene practices
- household dust.

Several other questions also show some effectiveness:

- pets
- household location (urban vs non-urban)
- dietary behaviors (organic food)
- exposure levels of household members
- health status (diseases)
- smoking behaviors
- proximity to agricultural fields (for house dust only).

The number of relationships evaluated in the publications for this second group of questions is small, indicating that their effectiveness has not been tested as extensively as for the questions in the first group.

For urine measurements, questions showing usefulness as indicators of a child's pesticide exposure level cover the areas of residential pesticide use both indoors and outdoors, household occupation, subject's personal characteristics, family hygiene practices, and smoking behavior. Each of these indicators seems plausible, in that such relationships have been seen in previous investigations of environmental exposures (e.g., lead exposure in children). The smoking questions appeared only in Krinsley (1998), whose study population was focused on adults, but included children greater than 10 years of age. Although second-hand smoke is noted as a significant predictor, the age of the majority of the study population and the very limited transferability of any pesticides from the smoke makes this question less effective for purposes of this project. For dust measurements, the questions showing usefulness as indicators of a child's pesticide exposure level cover the areas of household occupation, residential proximity to spraying, and family hygiene behavior. Each of these indicators also seems plausible in terms of pesticides being present in the child's environment. These questions represent potential exposure from the take-home pathway and from agricultural pesticide spraying.

The set of question categories used in this report (Table 4.2.3) provide one perspective for organizing the relationships. Three risk or exposure factors, related to the take-home or para-occupational exposure pathway, were analyzed as separate categories in this report: household occupation, family hygiene practices, and work exposure/practices. Household occupation is considered a source that may result in measurable differences in children's pesticide exposures. Most of the questions in this category involve the occupational status of household members. The occupations considered were pesticide applicators, farm workers, pesticide handlers, growers, and reference groups (non-agricultural workers). The occupation of household workers within the agricultural sector produced a substantial number of statistically significant relationships for urine and dust and the corresponding DAPs and OP parent compound levels. For these relationships, occupation may represent a surrogate for the actual exposure levels of household members employed in agriculture. These workers become reservoirs for the chemicals to which they are exposed at work. They subsequently transfer these chemicals into their homes and to their family members. This para-occupational exposure pathway involves the transport of contaminants from the workplace to the residence on a worker's clothing or person (Curl 2002). Children may be exposed to agricultural chemicals through the take-home or para-occupational pathway and their exposure levels are dependent on the occupational status, work, handling, and hygiene practices of agricultural workers in their households.

Two other risk factors examined in this report also contribute to the para-occupational exposure pathway. Family hygiene practices and work exposure/practices are considered behavioral practices that may modify pesticide exposure to agricultural workers and their family members. There were fewer relationships in these two categories because of the nature of the studies analyzed. The studies under review were primarily environmental exposures studies conducted in agricultural communities with a focus on children. If these studies had been strictly occupational exposure assessment studies, more questions related to the work and family hygiene practices might have been included in these studies. The findings which produced significant results such as laundering practices, vacuuming, and removal of work clothing and boots are also integral components required to fully understand the para-occupational exposure pathway.

4.3 Children's Pesticide Exposure Study (Yuma Study)

The second approach for evaluating questions useful in differentiating children's pesticide exposure levels was based on information available from a recent exposure study with this goal. The Children's Pesticide Exposure Study collected questionnaire responses and sample measurements from 152 households in Yuma County, Arizona. Throughout this section, the Children's Pesticide Exposure Study will be referred to as the Yuma Study.

In the Yuma Study, one child in each household was considered the principal participant. Urine samples were collected from the principal participant and a dust sample was collected from the household. An interview was conducted regarding the household's characteristics and activities, and the principal participant's behaviors. Siblings from the household were included in the study if they were available and in the appropriate age range (2-11 years old); however, only urine samples and minimal demographic information were collected for the siblings. For 77 of the households, one sibling was included in the study, and for 15 of the households two siblings were included.

The study design initially focused the selection of households on eight schools and of principal participants in kindergarten and first grade (Table 4.3.1). Seventeen children outside the initial school and grade list were included as principal participants. There were five "other" school categories including none. There were five "other" grade categories including: second grade, third grade, Head Start, preschool, and none.

Table 4.3.1 Number of Yuma Study Principal Participants, by School and Grade Level

	Grade of Principal Child			Total
School Attended by Principal Child	**Kindergarten**	**First Grade**	**Other Grades**	
School # 1	6	4	1	11
School # 2	16	25	0	41
School # 3	5	8	1	14
School # 4	4	6	0	10
School # 5	12	7	3	22
School # 6	3	8	0	11
School # 7	16	10	1	27
School # 8	4	1	0	5
Other Schools	1	0	10	11
Total	67	69	16	152

Urine samples were measured for the six dialkylphosphates: DEP, DETP, DEDTP, DMP, DMTP, and DMDTP. Unadjusted urinary metabolite measurements were available for 150 of the 152 principal participants; urinary metabolite measurements adjusted for creatinine were available for 148 of the 152 principal participants. Household dust samples were available for the 152 households. Dust samples were also collected from rooms where principal participants attended class in the six schools that gave permission (Table 4.3.2). School dust measurements were available for a subset of the schools and grades. These samples cover 82% of the principal participants from the eight schools in the initial Yuma Study design.

Table 4.3.2 Number of Principal Participants Where Yuma Study Dust Samples Were Collected, by School and Grade Level

	Grade of Principal Child		Total
School Attended by Principal Child	**Kindergarten**	**First Grade**	
School # 1	6	4	10
School # 2	16	25	41
School # 3	5	8	13
School # 4	4	6	10
School # 6	3	8	11
School # 7	16	10	26
Total	50	61	111

Household and school dust samples were measured for pesticides in the classes organophosphates, organochlorines, permethrins, and miscellaneous (Table 4.3.3).

Table 4.3.3 Pesticides Measured in Yuma Study Household and School Dust Samples

atrazine	4,4-' DDT	methyl parathion[a]
azinphos-methyl[a]	diazinon[a]	methoxychlor
bendiocarb	dichlorvos[a]	metolachlor
bensulide	dicofol	pendimethalin
benzamide	dieldrin	cis-permethrin
captan	disulfoton[a]	trans-permethrin
carbaryl	endosulfan 1	o-phenylphenol
carbofuran	endosulfan 2	phorate[a]
alpha-chlordane	ethyl parathion[a]	prometryn
gamma-chlordane	folpet	propoxur
chlorpyrifos[a]	fonophos[a]	simazine
chlorthal-dimethyl	heptachlor	terbufos[a]
cy-permethrin	hexachlorobenzene	trifluralin
4,4-' DDD	lindane	
4,4-' DDE	malathion[a]	

[a] Organophosphorous (OP) pesticides

Relationships found in the Yuma Study are described in two segments. Section 4.3.1 describes the relationships that are relevant to the interests of this project, based on the Yuma Study report (CDC 2002). Section 4.3.2 and Appendix G describe the relationships identified from the data mining analysis. Both analysis paths use the same study data set, but consider different subsets of the Yuma Study participants, and performed analyses for different purposes. These differences should be taken into consideration when comparing results from the two approaches.

4.3.1 Relationships Explored in the Yuma Study Report

The Yuma Study analyzed potential risk factors, based on the questionnaire responses, for children in a household, that is, the principal participant and any siblings. The objective of the study was to determine the effect and levels of pesticide exposure on children living or attending schools near pesticide-treated fields (CDC 2002). A child's exposure level was determined by the level of pesticide metabolites in the urine. The study's report uses the terms risk factors, associations, and borderline, and those terms will be used in section 4.3.1 when describing the report's results. For purposes of this report, the terms risk (or exposure) factors and questions, association and relationship, and borderline and marginal (regarding statistical significance) are interchangeable in section 4.3.

4.3.1.1 Relationships Between Questions and DAP Metabolites

For the Yuma Study report (CDC 2002), the children's exposure levels were evaluated with regression models controlled for intra-household correlation with household as the repeated measurement. The potential risk factors selected for analysis were the subset of the full set of questions that could be applied to, and were available for, siblings as well as principal participants. These factors included the child's physical characteristics and household characteristics or practices. Child-specific behaviors were not used for the analyses because they were not collected on any siblings. The pesticide metabolite concentrations were log transformed to better meet the normality assumptions of the analyses and generalized estimating equations (SAS version 8.2, SAS Institute, Cary, NC) were used to measure the associations. Discussions about whether to analyze urinary metabolites in children as adjusted or unadjusted for creatinine can be found in the literature, e.g., O'Rourke (2000).

Table 4.3.4 Results of Regression Models[a] with DMOP and DEOP, Unadjusted and Adjusted for Creatinine, for 152 Households

Risk Factor	DMOP[b] unadj[c] Slope[f] (p-value)[g]	DMOP[b] adj[d] Slope[f] (p-value)[g]	DEOP[e] unadj[c] Slope[f] (p-value)[g]	DEOP[e] adj[d] Slope[f] (p-value)[g]
Sex of participant	-0.07 (0.68)	-0.21 (0.25)	0.01 (0.94)	-0.12 (0.30)
Age of participant	-0.02 (0.70)	-0.06 (0.23)	-0.01 (0.71)	-0.05 (0.21)
Size of participant	0.00 (0.98)	0.00 (0.94)	-0.03 (0.40)	-0.02 (0.49)
Use of lice shampoo in last year	0.06 (0.78)	-0.01 (0.98)	-0.07 (0.67)	-0.13 (0.56)
Distance from home to agricultural field	0.18 (0.36)	-0.05 (0.82)	0.00 (0.99)	-0.23 (0.12)
Use of pesticides inside home in last month	0.03 (0.87)	0.27 (0.16)	**0.23 (0.06)**	***0.45 (0.00)***
Use of pesticides outside of home in last month	0.19 (0.31)	0.31 (0.11)	0.14 (0.25)	0.24 (0.10)
Father working in agriculture	-0.12 (0.54)	-0.19 (0.33)	-0.03 (0.83)	-0.11 (0.49)
Mother working in agriculture	0.27 (0.54)	0.19 (0.68)	**0.44 (0.06)**	0.39 (0.18)
Father or mother working in agriculture	0.09 (0.84)	-0.22 (0.63)	0.04 (0.86)	-0.24 (0.42)
Other adult in house working in agriculture	-0.19 (0.46)	-0.30 (0.22)	-0.23 (0.23)	***-0.32 (0.04)***
Father, mother or other adult working in agriculture	-0.23 (0.56)	0.46 (0.25)	0.00 (0.99)	-0.20 (0.46)

[a] Regression model included all participating children controlling for intra-household correlation with household as a repeated measure. Slope and p-value provided. N varies according to available responses for a risk factor.
[b] DMOP is a summary variable made from summing molar weights of DMP, DMTP, and DMDTP. (Concentrations < Limit of detection (LOD) were replaced with LOD/2.)
[c] Unadjusted for creatinine (ug/l urine).
[d] Adjusted for creatinine (ug/g Creatinine).
[e] DEOP is a summary variable made from summing molar weights of DEP, DETP, and DEDTP. (Concentrations < LOD were replaced with LOD/2.)
[f] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values (p < 0.05) are in bold italics. Slopes associated with borderline statistically significant p-values (0.05 ≤ p < 0.10) are in bold. For questions answered by a yes or no, a yes response was assigned a value of 1 and a no response was assigned a value of 2.
[g] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values (0.05 ≤ p <0.10) are in bold.

No risk factors were found to be associated with DMOP, the sum of methylated DAPs (Table 4.3.4). For DEOP, the sum of ethylated DAPs, the strongest association is with the questions for *recent pesticide use in the home*. Secondary associations are identified with questions about *the mother or another adult (not father) working in agriculture,* which may relate to the level of daily interactions between these adults and the children. The coding assigned to the yes and no responses was 1 and 2, respectively. Thus, negative slopes indicate that the "yes" respondents have a higher measurement level than the "no" respondents, and positive slopes indicate that the "yes" respondents have a lower measurement level than the "no" respondents. Some of the slopes are in the direction expected (negative slope) based on current knowledge, while others like *recent pesticide use in the home* or *mother working in agriculture* appear to be in the reverse direction (positive slope). Alternatively, the reverse direction for *mother working in agriculture* may be a surrogate measure for time away from home rather than the take-home pathway.

Statistical analyses were also performed on the individual DAPs, and in a few instances, risk factors that are significant or marginally significant for an individual DAP metabolite are not significant for the metabolite sum. One such example is *recent pesticide use in the home* for methylated DAPs. There is a significant association for DMP, and no significant association for DMTP, DMDTP and DMOP (Tables 4.3.4 and 4.3.5). This might indicate the impact of combining associations having different directions of association or of combining strong and weak associations.

Table 4.3.5 Results of Regression Models[a] with Individual DAP Metabolites, Unadjusted and Adjusted for Creatinine, for 152 Households

Risk factor	DMP Slope[b] (p-value)[c]	DMTP Slope[b] (p-value)[c]	DMDTP Slope[b] (p-value)[c]	DEP Slope[b] (p-value)[c]	DETP Slope[b] (p-value)[c]	DEDTP Slope[b] (p-value)[c]
	Unadjusted for Creatinine[d]					
Sex of participant	-0.01 (0..96)	-0.15 (0.46)	0.02 (0.93)	-0.02 (0.85)	0.00 (0.97)	0.12 (0.31)
Age of participant	-0.02 (0.69)	0.05 (0.44)	0.04 (0.62)	-0.03 (0.41)	-0.00 (0.87)	***0.07 (0.03)***
Size of participant	-0.05 (0.27)	0.05 (0.44)	-0.03 (0.79)	-0.04 (0.26)	-0.02 (0.62)	-0.00 (0.97)
Use of lice shampoo in last year	-0.01 (0.95)	0.26 (0.41)	-0.12 (0.78)	-0.07 (0.73)	-0.14 (0.19)	0.09 (0.70)
Distance from home to agricultural field	0.08 (0.66)	0.10 (0.72)	0.31 (0.37)	-0.07 (0.63)	-0.00 (0.99)	***0.30 (0.02)***
Use of pesticides inside home in last month	***0.39 (0.02)***	-0.04 (0.87)	-0.12 (0.70)	***0.31 (0.03)***	**0.19 (0.09)**	-0.22 (0.13)
Use of pesticides outside of home in last month	0.12 (0.49)	0.17 (0.52)	0.16 (0.64)	0.18 (0.22)	0.06 (0.57)	-0.21 (0.16)
Father working in agriculture	-0.30 (0.12)	-0.02 (0.95)	0.16 (0.65)	-0.13 (0.41)	0.07 (0.58)	0.27 (0.11)
Mother working in agriculture	**0.67 (0.08)**	0.32 (0.57)	1.27 (0.10)	0.39 (0.16)	0.28 (0.22)	**0.87 (0.08)**
Father or mother working in agriculture	-0.33 (0.32)	0.09 (0.88)	***1.46 (0.04)***	-0.08 (0.77)	0.09 (0.68)	0.53 (0.16)
Other adult in house working in agriculture	-0.21 (0.39)	-0.64 (0.11)	0.14 (0.77)	**-0.34 (0.08)**	-0.16 (0.29)	0.33 (0.30)

Risk factor	DMP Slope[b] (p-value)[c]	DMTP Slope[b] (p-value)[c]	DMDTP Slope[b] (p-value)[c]	DEP Slope[b] (p-value)[c]	DETP Slope[b] (p-value)[c]	DEDTP Slope[b] (p-value)[c]
Father, mother or other adult working in agriculture	-0.19 (0.56)	-0.67 (0.25)	0.44 (0.51)	-0.06 (0.83)	0.01 (0.97)	0.35 (0.30)
	Adjusted for Creatinine[e]					
Sex of participant	-0.14 (0.43)	-0.29 (0.18)	-0.10 (0.71)	-0.15 (0.30)	-0.14 (0.16)	-0.01 (0.97)
Age of participant	-0.05 (0.35)	-0.00 (0.98)	-0.00 (0.97)	-0.07 (0.14)	-0.04 (0.20)	0.03 (0.31)
Size of participant	-0.05 (0.37)	0.06 (0.39)	-0.02 (0.86)	-0.04 (0.39)	-0.02 (0.63)	0.00 (0.93)
Use of lice shampoo in last year	-0.07 (0.82)	0.17 (0.65)	-0.20 (0.63)	-0.13 (0.63)	-0.20 (0.19)	0.03 (0.89)
Distance from home to agricultural field	-0.14 (0.53)	-0.18 (0.53)	0.05 (0.89)	**-0.31 (0.08)**	**-0.22 (0.05)**	0.06 (0.67)
Use of pesticides inside home in last month	***0.61 (0.00)***	0.25 (0.33)	0.15 (0.63)	***0.53 (0.00)***	***0.40 (0.00)***	0.01 (0.94)
Use of pesticides outside of home in last month	0.21 (0.32)	0.34 (0.19)	0.31 (0.33)	0.28 (0.11)	0.15 (0.18)	-0.10 (0.47)
Father working in agriculture	**-0.38 (0.09)**	-0.10 (0.71)	0.08 (0.81)	0.22 (0.25)	-0.00 (0.99)	0.19 (0.23)
Mother working in agriculture	0.63 (0.17)	0.18 (0.75)	1.14 (0.14)	0.33 (0.34)	0.23 (0.35)	0.79 (0.11)
Father or mother working in agriculture	-0.60 (0.14)	-0.30 (0.63)	1.10 (0.11)	-0.37 (0.25)	-0.17 (0.42)	0.23 (0.57)
Other adult in house working in agriculture	-0.30 (0.22)	***-0.76 (0.03)***	0.02 (0.96)	***-0.44 (0.02)***	***-0.25 (0.02)***	0.23 (0.44)
Father, mother or other adult working in agriculture	-0.37 (0.33)	**-0.99 (0.07)**	0.14 (0.82)	-0.27 (0.39)	-0.17 (0.38)	0.13 (0.71)

[a] Regression model included all participating children controlling for intra-household correlation with household as a repeated measure. Slope and p-value provided. N varies according to available responses for a risk factor. (Concentrations < LOD were replaced by LOD/2.)
[b] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values ($p < 0.05$) are in bold italics. Slopes associated with borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold. For questions answered by a yes or no, a yes response was assigned a value of 1 and a no response was assigned a value of 2.
[c] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold.
[d] ug/l urine.
[e] ug/g Creatinine.

When looking at the individual DAPs, associations of the methylated DAPs occur with the questions about *recent pesticide use in the home* and *household members working in agriculture* (Table 4.3.5). As expected, based on the significant associations for DEOP (Table 4.3.4), these risk factors are associated with some of the individual ethylated DAPs, DEP and DETP (Table 4.3.5). *Distance from home to agricultural fields* also shows significant associations with DEP and DETP (Table 4.3.5). The significant associations with these two DAPs are likely the basis for the significant relationships with DEOP (Table 4.3.4).

The positive valued slopes for the questions with yes/no responses show an association opposite of what might be expected for the risk factor, that is, a yes response is predicted to have a lower measurement level than a no response.

Statistical analyses were also performed on the risk factor *distance from household to agricultural field*. The households were divided into two groups, those whose distance to the agricultural fields was < 250 feet, and those whose distance was ≥ 250 feet. The question *distance from home to the agricultural fields* for principal participants shows statistical significance (borderline) only for the DEDTP metabolite, with distances closer to the agricultural fields having higher concentration values, as expected (Table 4.3.6).

Table 4.3.6 Results Comparing Distance from Home to Agricultural Fields with Six DAP Metabolites, Unadjusted and Adjusted for Creatinine, for Principal Participants

Analyte (unadjusted, ug/l urine) (adjusted, ug/g Creatinine)	N_1	**Mean and range of urine samples in area < 250 feet**[a]	N_2	**Mean and range of urine samples in area ≥ 250 feet**[a]	**t-statistic**	**p-value**
DMP (unadjusted)	108[b]	4.06 (0.29 – 29.00)	42	3.33 (0.29 – 14.00)	1.00	0.32
DMP (adjusted)	107[c]	7.21 (0.18 – 60.13)	41[d]	6.67 (0.28 – 49.82)	0.31	0.76
DMTP (unadjusted)	108[b]	13.43 (0.09 – 200.00)	42	11.10 (0.09 – 120.00)	0.48	0.63
DMTP (adjusted)	107[c]	21.15 (0.09 – 409.00)	41[d]	18.10 (0.30 – 223.33)	0.36	0.72
DMDTP (unadjusted)	108[b]	5.61 (0.04 – 160.00)	42	4.02 (0.04 – 51.00)	0.67	0.50
DMDTP (adjusted)	107[c]	8.78 (0.02 – 215.25)	41[d]	6.71 (0.03 – 94.29)	0.53	0.59
DEP (unadjusted)	108[b]	3.24 (0.59 – 21.00)	42	2.92 (0.55 – 11.00)	0.57	0.57
DEP (adjusted)	107[c]	5.37 (0.41 – 40.32)	41[d]	5.61 (0.81 – 39.15)	-0.19	0.85
DETP (unadjusted)	108[b]	1.32 (0.50 – 5.70)	42	1.73 (0.50 – 9.2)	-1.32	0.19
DETP (adjusted)	107[c]	2.04 (0.24 – 9.09)	41[d]	2.42 (0.67 – 10.53)	-1.16	0.25
DEDTP (unadjusted)	108[b]	0.50 (0.08 – 14.00)	42	0.24 (0.08 – 1.10)	1.71	0.09
DEDTP (adjusted)	107[c]	0.64 (0.07 – 11.75)	41[d]	0.39 (0.06 – 1.42)	1.62	0.11

[a] Concentrations < LOD were replaced with LOD/2.
[b] Results from urine samples of two principal participants were not available.
[c] Results from urine samples of two principal participants were not available and creatinine level from urine sample of one principal participant was not reported.
[d] Creatinine level from urine sample of one principal participant was not reported.

4.3.1.2 Relationships Between Dust Measurements and DAP Metabolites

The Yuma Study (CDC 2002) evaluated associations between the DAP metabolite levels and levels of the ten pesticides most detected in the household dust samples. The associations were evaluated with the ethylated (DEOP) and methylated (DMOP) DAP sums, adjusted and unadjusted for creatinine (Table 4.3.7), and for the six individual DAPs, adjusted and unadjusted for creatinine (Table 4.3.8).

Table 4.3.7 Results of Regression Models[a] with DMOP and DEOP, Unadjusted and Adjusted for Creatinine, and the Ten Pesticides Most Detected in Household Dust Samples for 152 Households

Household dust pesticide	DMOP[b] unadj[c] Slope[f] (p-value)[g]	DMOP[b] adj[d] Slope[f] (p-value)[g]	DEOP[e] unadj[c] Slope[f] (p-value)[g]	DEOP adj[d] Slope[f] (p-value)[g]
Trans-permethrin	0.00 (0.23)	***0.00 (0.03)***	**0.00 (0.07)**	**0.00 (0.06)**
Cis-permethrin	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.03)***
Chlorpyrifos	***-0.00 (0.00)***	***-0.00 (0.03)***	0.00 (0.20)	***0.00 (0.01)***
Diazinon	-0.00 (0.32)	**-0.00 (0.06)**	***-0.00 (0.00)***	0.00 (0.14)
Propoxur	***-0.00 (0.00)***	-0.00 (0.61)	***-0.00 (0.00)***	***0.00 (0.01)***
O-phenylphenol	-0.00 (0.92)	0.00 (0.92)	0.00 (0.59)	-0.00 (0.44)
Cy-permethrin	**-0.00 (0.07)**	-0.00 (0.10)	**0.00 (0.06)**	***0.00 (0.00)***
4,4'-DDT	***-0.00 (0.01)***	-0.00 (0.49)	-0.00 (0.18)	0.00 (0.54)
Gamma-chlordane	-0.00 (0.66)	0.00 (0.84)	**-0.00 (0.05)**	**-0.00 (0.07)**
Carbaryl	***0.00 (0.00)***	***0.00 (0.00)***	**-0.00 (0.09)**	***-0.00 (0.00)***

[a] Regression model included all participating children controlling for intra-household correlation with household as a repeated measure. Slope and p-value provided. N varies according to available responses for a risk factor.
[b] DMOP is a summary variable made from summing molar weights of DMP, DMTP, and DMDTP. (Concentrations < LOD were replaced with LOD/2.)
[c] Unadjusted for creatinine (ug/l urine).
[d] Adjusted for creatinine (ug/g Creatinine).
[e] DEOP is a summary variable made from summing molar weights of DEP, DETP, and DEDTP. (Concentrations < LOD were replaced with LOD/2.)
[f] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values ($p < 0.05$) are in bold italics. Slopes associated with borderline statistically significant p-values ($0.05 \leq p < 0.10$) are in bold.
[g] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values ($0.05 \leq p < 0.10$) are in bold.

Table 4.3.8 Results of Regression Models[a] with Individual DAP Metabolites, Unadjusted and Adjusted for Creatinine, and the Ten Pesticides Most Detected in Household Dust Samples for 152 Households

Household dust pesticide	DMP Slope[b] (p-value)[c]	DMTP Slope[b] (p-value)[c]	DMDTP Slope[b] (p-value)[c]	DEP Slope[b] (p-value)[c]	DETP Slope[b] (p-value)[c]	DEDTP Slope[b] (p-value)[c]
	Unadjusted for Creatinine[d]					
Trans-permethrin	0.00 (0.10)	0.00 (0.171)	**0.00 (0.07)**	***0.00 (0.01)***	0.00 (0.44)	-0.00 (0.60)
Cis-permethrin	***0.00 (0.01)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	**0.00 (0.07)**	-0.00 (0.76)
Chlorpyrifos	-0.00 (0.22)	***-0.00 (0.05)***	0.00 (0.24)	0.00 (0.20)	0.00 (0.10)	-0.00 (0.13)
Diazinon	0.00 (0.33)	-0.00 (0.13)	-0.00 (0.12)	***0.00 (0.00)***	***0.00 (0.00)***	0.00 (0.74)
Propoxur	**0.00 (0.00)**	-0.00 (0.42)	-0.00 (0.62)	***-0.00 (0.00)***	**-0.00 (0.07)**	**-0.00 (0.08)**
O-phenylphenol	0.00 (0.30)	-0.00 (0.94)	-0.00 (0.29)	-0.00 (0.72)	-0.00 (0.89)	***-0.00 (0.00)***
Cy-permethrin	-0.00 (0.52)	-0.00 (0.31)	-0.00 (0.68)	**0.00 (0.08)**	***0.00 (0.02)***	***-0.00 (0.04)***
4,4'-DDT	-0.00 (0.43)	***-0.00 (0.03)***	***-0.00 (0.00)***	-0.00 (0.48)	***-0.00 (0.02)***	-0.00 (0.64)
Gamma-chlordane	0.00 (0.32)	0.00 (0.62)	0.00 (0.52)	**-0.00 (0.05)**	**-0.00 (0.09)**	0.00 (0.97)
Carbaryl	-0.00 (0.30)	***0.00 (0.01)***	-0.00 (0.85)	-0.00 (0.17)	***-0.00 (0.01)***	-0.00 (0.89)
	Adjusted for Creatinine[e]					
Trans-permethrin	0.00 (0.17)	***0.00 (0.01)***	***0.00 (0.00)***	**0.00 (0.07)**	***0.00 (0.00)***	-0.00 (0.82)
Cis-permethrin	0.00 (0.13)	***0.00 (0.00)***	***0.00 (0.00)***	**0.00 (0.05)**	***0.00 (0.00)***	-0.00 (0.98)
Chlorpyrifos	-0.00 (0.14)	-0.00 (0.24)	0.00 (0.20)	***0.00 (0.03)***	***0.00 (0.00)***	-0.00 (0.41)
Diazinon	-0.00 (0.89)	***-0.00 (0.03)***	***-0.00 (0.02)***	0.00 (0.23)	***0.00 (0.03)***	0.00 (0.41)
Propoxur	0.00 (0.49)	***0.00 (0.02)***	0.00 (0.26)	0.00 (0.16)	***0.00 (0.00)***	***0.05 (0.03)***
O-phenylphenol	-0.00 (0.24)	0.00 (0.39)	-0.00 (0.48)	-0.00 (0.55)	-0.00 (0.59)	***-0.00 (0.00)***
Cy-permethrin	0.00 (0.73)	-0.00 (0.48)	0.00 (0.99)	***0.00 (0.00)***	***0.00 (0.02)***	-0.00 (0.51)
4,4'-DDT	0.00 (0.58)	-0.00 (0.41)	***-0.00 (0.01)***	-0.00 (0.44)	-0.00 (0.98)	-0.00 (0.44)
Gamma-chlordane	0.00 (0.47)	0.00 (0.77)	0.00 (0.62)	**-0.00 (0.08)**	***-0.00 (0.04)***	0.00 (0.82)

Household dust pesticide	DMP Slope[b] (p-value)[c]	DMTP Slope[b] (p-value)[c]	DMDTP Slope[b] (p-value)[c]	DEP Slope[b] (p-value)[c]	DETP Slope[b] (p-value)[c]	DEDTP Slope[b] (p-value)[c]
Carbaryl	-0.00 (0.10)	**0.00 (0.05)**	0.00 (0.57)	***0.00 (0.00)***	***-0.00 (0.00)***	**-0.00 (0.06)**

[a] Regression model included all participating children controlling for intra-household correlation with household as a repeated measure. Slope and p-value provided. N varies according to available responses for a risk factor.
[b] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values ($p < 0.05$) are in bold italics. Slopes associated with borderline statistically significant p-values ($0.05 \leq p < 0.10$) are in bold.
[c] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values ($0.05 \leq p < 0.10$) are in bold.
[d] ug/l urine.
[e] ug/g Creatinine.

The Yuma Study (CDC 2002) also evaluated associations between the DAP urinary metabolite levels and the levels of the seven pesticides most detected across the household and school dust samples. The associations were evaluated with the ethylated (DEOP) and methylated (DMOP) DAP sums, adjusted and unadjusted for creatinine (Table 4.3.9), and for the six individual DAPs, adjusted and unadjusted for creatinine (Table 4.3.10). The statistical analyses were performed only for the principal participants whose school/classroom dust was measured, that is, in only six of the eight schools from the initial study design (Table 4.3.2).

Table 4.3.9 Results of Regression Models[a] with DMOP and DEOP, Unadjusted and Adjusted for Creatinine, and the Seven Pesticides Most Detected in Household and School Dust Samples, for Principal Participants

Household and school dust pesticide	DMOP[b] unadj[c] Slope[f] (p-value)[g]	DMOP[b] adj[d] Slope[f] (p-value)[g]	DEOP[e] unadj[c] Slope[f] (p-value)[g]	DEOP[e] adj[d] Slope[f] (p-value)[g]
Trans-permethrin (n[h] = 80/n[i] =79)	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***
Cis-permethrin (n[h] = 82/n[i] =81)	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***
Chlorpyrifos (n[h] = 110/n[i] =108)	-0.00 (0.15)	-0.0 (0.28)	0.00 (0.45)	0.00 (0.18)
Diazinon (n[h] = 110/n[i] =108)	-0.00 (0.14)	***-0.00 (0.01)***	***-0.00 (0.00)***	0.00 (0.11)
Propoxur (n[h] = 110/n[i] =108)	-0.00 (0.56)	0.00 (0.32)	***-0.00 (0.00)***	0.00 (0.20)
O-phenylphenol (n[h] = 110/n[i] =108)	-0.00 (0.74)	0.00 (0.76)	-0.00 (0.97)	-0.00 (0.96)
Cy-permethrin (n[h] = 79/n[i] =77)	-0.00 (0.27)	**-0.00 (0.06)**	***-0.00 (0.01)***	***-0.00 (0.00)***

[a] Regression model included only principal participants where school dust samples were collected from their classrooms. Slope and p-value provided.

[b] DMOP is a summary variable made from summing molar weights of DMP, DMTP, and DMDTP. (Concentrations < LOD were replaced with LOD/2.)
[c] Unadjusted for creatinine (ug/l urine).
[d] Adjusted for creatinine (ug/g Creatinine).
[e] DEOP is a summary variable made from summing molar weights of DEP, DETP, and DEDTP. (Concentrations < LOD were replaced with LOD/2.)
[f] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values ($p < 0.05$) are in bold italics. Slopes associated with borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold.
[g] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold.
[h] Number of measurements unadjusted for creatinine.
[i] Number of measurements adjusted for creatinine.

Table 4.3.10 Results of Regression Models[a] with Individual DAP Metabolites, Unadjusted and Adjusted for Creatinine, and the Seven Pesticides Most Detected in Household and School Dust Samples, for Principal Participants

Household and school dust pesticide	DMP Slope[b] (p-value)[c]	DMTP Slope[b] (p-value)[c]	DMDTP Slope[b] (p-value)[c]	DEP Slope[b] (p-value)[c]	DETP Slope[b] (p-value)[c]	DEDTP Slope[b] (p-value)[c]
	Unadjusted for Creatinine[d]					
Trans-permethrin (n = 80)	***0.00 (0.01)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***
Cis-permethrin (n = 82)	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	0.00 (0.20)
Chlorpyrifos (n = 110)	***-0.00 (0.00)***	-0.00 (0.53)	0.00 (0.29)	0.00 (0.61)	0.00 (0.15)	-0.00 (0.51)
Diazinon (n = 110)	0.00 (0.84)	-0.00 (0.33)	-0.00 (0.33)	***0.00 (0.00)***	***-0.00 (0.00)***	***-0.00 (0.00)***
Propoxur (n=110)	***-0.00 (0.00)***	-0.00 (0.22)	**0.00 (0.07)**	***-0.00 (0.00)***	-0.00 (0.87)	-0.00 (0.31)
O-phenylphenol (n = 110)	-0.00 (0.41)	-0.00 (0.61)	-0.00 (0.65)	-0.00 (0.79)	-0.00 (0.63)	***-0.00 (0.01)***
Cy-permethrin (n = 79)	-0.00 (0.57)	0.00 (0.22)	***-0.00 (0.01)***	***0.00 (0.00)***	***0.00 (0.01)***	***0.00 (0.01)***
	Adjusted for Creatinine[e]					
Trans-permethrin (n = 79)	***0.00 (0.01)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	0.00 (0.63)
Cis-permethrin (n = 81)	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.00)***	0.00 (0.81)
Chlorpyrifos (n= 108)	***-0.00 (0.01)***	-0.00 (0.53)	0.00 (0.29)	0.00 (0.40)	***0.00 (0.01)***	0.00 (0.77)
Diazinon (n= 108)	-0.00 (0.21)	-0.00 (0.62)	0.00 (0.22)	0.00 (0.24)	***0.00 (0.00)***	***-0.00 (0.00)***
Propoxur (n= 108)	**-0.00 (0.07)**	***0.00 (0.03)***	**0.00 (0.07)**	0.00 (0.58)	***0.00 (0.00)***	***0.00 (0.04)***
O-phenylphenol (n= 108)	-0.00 (0.38)	0.00 (0.52)	0.00 (0.76)	0.00 (0.91)	-0.00 (0.40)	-0.00 (0.65)
Cy-permethrin (n = 77)	-0.00 (0.47)	0.00 (0.38)	***-0.00 (0.00)***	***0.00 (0.00)***	***0.00 (0.01)***	***-0.00 (0.00)***

[a] Regression model included only principal participants where school dust samples were collected from their classrooms. Slope and p-value provided. (Concentrations < LOD were replaced by LOD/2.)
[b] The slope estimates the increase in the pesticide level per unit increase in the independent variable. Slopes associated with statistically significant p-values ($p < 0.05$) are in bold italics. Slopes associated with borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold.
[c] Statistically significant p-values (<0.05) are in bold italics. Borderline statistically significant p-values ($0.05 \le p < 0.10$) are in bold.
[d] ug/l urine.
[e] ug/g Creatinine.

Many associations between the DAP urinary metabolites and the most detected OP pesticides in household and school dust were found; however, the regression coefficients are very small

(Tables 4.3.7 – 4.3.10). Thus, the associations may be statistically significant, but may not necessarily be practically significant. The report authors note:

> The regression models in which the slopes were small but were statistically significant may suggest either that a) true associations existed, but the numbers of significance were less than the numbers measured in the statistical programs or b) the associations were meaningless and based solely [on] the probability of finding statistical significance if enough tests were run. (CDC 2002)

Some of the most detected pesticides in household and school dust samples are other than OP pesticides and associations between the DAPs and pesticides exist regardless of the class of pesticide. These relationships may indicate heavy pesticide use, although they do not correspond to the metabolites found.

4.3.1.3 Summary of Results

The analyses from the Yuma Study report (CDC 2002) show that the most significant associations with DAP urinary metabolites are questions about *recent pesticide use in the home*, *adult household members working in agriculture*, and *distance from home to agricultural fields*. Table 4.3.11 summarizes the significant associations between questions and DAP metabolites based on Tables 4.3.4, 4.3.5, and 4.3.6. Not all of the significant associations are in the directions expected. In some cases, it is either the concentration adjusted, or unadjusted, for creatinine that is significant, but not both. O'Rourke (2000) and Barr (2004) include discussions about differences in the use of the two measures for statistical analysis.

Questions about *recent pesticide use in the home*, *take-home pathway from the mother or other adult working in agriculture*, and *distance from home to agricultural fields* seem to be the most useful in predicting ethylated DAP exposure measurements in urine. Questions about the *father working in agriculture* seem to be somewhat useful in predicting methylated DAP exposure measurements, which is to be expected since methylated OPs are commonly used in agriculture. In many of the associations, however, the direction of the association is the opposite of what is expected (Table 4.3.11). Many strong associations are shown between the pesticides most detected in household and school dust samples and the DAP metabolites. Most of the significant regression coefficients are in the direction expected for the association based on current knowledge.

Table 4.3.11 Questions and DAP Metabolites with Significant[a] Relationships in the Yuma Study Based on Tables 4.3.4, 4.3.5, and 4.3.6

Questions	DAP Metabolites[b]															
	DEP		DETP		DEDTP		DEOP[c]		DMP		DMTP		DMDTP		DMOP[d]	
	u[e]	a[e]	u	a	u	a	u	a	u	a	u	a	u	a	u	a
Age of participant					X											
Used pesticide inside home in last month	X	X	X	X			X	X	X	X						
Distance from home to agricultural field		Y		Y	X											
Mother working in agriculture					X		X		X							
Father working in agriculture										Y						
Father or mother working in agriculture													X			
Other adult in house working in agriculture	Y	Y		Y				Y				Y				
Father, mother or other adult working in agriculture												Y				

[a] Statistically significant or borderline significant.
[b] DEP = diethylphosphate, DETP = diethylthiophosphate, DEDTP = diethyldithiophosphate
DMP = dimethylphosphate, DMTP = dimethylthiophosphate, DMDTP = dimethyldithiophosphate.
[c] DEOP is a summary variable made from summing molar weights of DEP, DETP, and DEDTP. (Concentrations < LOD were replaced with LOD/2.)
[d] DMOP is a summary variable made from summing molar weights of DMP, DMTP, and DMDTP. (Concentrations < LOD were replaced with LOD/2.)
[e] u = unadjusted for creatinine.
a = adjusted for creatinine.
X = occurrence of risk factor associated with lower levels of pesticide metabolite.
Y = occurrence of risk factor associated with higher levels of pesticide metabolite.

4.3.2 Results from the Data Mining Approach

In the Yuma Study report (CDC 2002), hypotheses were defined a priori which set the direction for the data analyses performed. Based on these hypotheses, the risk factors were analyzed individually with the urinary DAP metabolites measured. The data mining approach provides options for exploring the Yuma Study data for relationships between risk factors and exposure levels without specifying a priori views, that is, based on relationships that exist in the data. In some cases, the risk factors were analyzed in groups and interactions between risk factors in the relationships were considered. In this section, the term relationships will be used instead of the term associations used in Section 4.3.1, to be consistent with the use of relationships in Section 4.2. Their meaning, however, is considered interchangeable.

4.3.2.1 Subpopulation Selected for Analysis

Since questionnaire responses and school dust measurements were not collected for siblings, the analyses reported here were performed only on data from principal participants. To further limit the impact of factors relating to children not defined in the initial study design, the principal participants from kindergarten and first grade and from the initial eight schools, were selected as the core set of participants for the data mining analysis. Comparisons of questionnaire responses between the 135 core participants (Table 4.3.12), and the other 17 participants (Table 4.3.1) showed little difference. Depending on the particular statistical analysis, and the urinary metabolite or sum selected as the dependent variable, up to five additional core participants were excluded because of a lack of, or suspicions about, the urinary metabolite measurements. Subsequent use of the phrase principal child will denote the core principal participant children described above.

Table 4.3.12 Number of Yuma Study Core Principal Participants, by School and Grade Level

	Grade of Principal Child		Total
School Attended by Principal Child	**Kindergarten**	**First Grade**	
School # 1	6	4	10
School # 2	16	25	41
School # 3	5	8	13
School # 4	4	6	10
School # 5	12	7	19
School # 6	3	8	11
School # 7	16	10	26
School # 8	4	1	5
Total	66	69	135

4.3.2.2 Preliminary Analyses

Two types of preliminary analyses were performed to begin understanding potential relationships: bivariate analyses to identify simple indicators of exposure level and principal component analysis to understand the underlying dimensions or structure in the data. These analyses are described in Appendix G, sections G.2.2.1 and G.2.2.2. The bivariate analyses included the principal participants with usable urinary metabolite measurements (approximately 148 children), and were performed before any recoding of questionnaire responses for conditional questions and non-responses (Appendix G, sections G.2.1.3 and G.2.1.4). Because the questions were used as categorical grouping variables, the lack of recoding did not affect the evaluation of the relationships. Questionnaire variables that indicate some differences in levels for at least three of the six DAP metabolites (DEP, DETP, DEDTP, DMP, DMTP, DMDTP) are:

Variable Name	Variable Description
cheminhs	Pesticides used inside home last month?
chemouth	Pesticides used outside home last month?
closeapp	Distance between home and nearest application of pesticides
washvegi	How often wash local fruit/veg before eating?
momwork	Mother now employed (not as housewife)?
insured	Is child covered by medical insurance?

Since house dust measurements are potential indicators of exposure, non-parametric correlations between the dust and urine measurements were also performed. Fourteen of the forty-three dust chemicals from Table 4.3.3 show some correlation with the urine measurements. Chlorpyrifos, diazinon, endosulfan I, endosulfan II, pendimethrin, trifuralin, and terbufos show a correlation with more than one of the DAP metabolites. The non-OPs in this list may be indicative of heavy pesticide use, although they do not correspond to the DAP metabolites.

4.3.2.3 Analysis for Underlying Structure

A principal component analysis (PCA) was performed to identify the dimensions (groups of questions) explaining the most variability among the potential predictors. When considering relationships of questions with urine measurements, questions in the same dimension can be considered like surrogate questions, although each question in a dimension is not a replacement for the information contained in the group of questions forming the dimension. Questionnaire responses were recoded to ensure that responses affected by a conditioning question would be analyzed appropriately (G.2.1.3). This type of recoding affects the questions included in a PCA dimension. For example, the question *cheminhs*, about pesticide treatment inside the house, is the condition question for all questions regarding specific rooms that were treated. This conditioning of the code values for the room-treated questions was a likely influence on all of the room questions being grouped together in one dimension.

Two scenarios were run in the PCA. One scenario was based on 67 of the questions in Table G.2.1; the other scenario was based on the same 67 questions and the 22 house and school dust measurement sums in Table G.2.4. Note that the number of cases used in the two PCA scenarios differ because school dust measurements were not available for all principal participants. The complete listing of the principal components (PCs), or dimensions, can be found in Table G.3.1 in Appendix G. The ten PCs explaining the most variability in the data for each scenario are listed in Table 4.3.13.

The dimensions explaining the most variability across the two scenarios were:

- Pesticide sprayed inside house
- School and school dust measurements
- Child working in agricultural field
- Relationship of home to agricultural fields
- House dust measurements--OPs
- Adults in household working with pesticides.

Although these dimensions were not analyzed with respect to the urine measurements, they are consistent with the findings in Stage 3 which were so analyzed. School dust measurements took prominence in the dimensions extracted when they were included in the second scenario. These dimensions are useful in understanding the relationships between questions or questions and dust measurements; however, they do not directly represent questions having statistically significant relationships with the urine measurement concentrations. They do represent sets of questions that have more variability, which may help differentiate pesticide metabolite levels.

Table 4.3.13 First Ten Principal Components[a] from Two Scenarios Using Yuma Study Data

	Questions-only Scenario (N=130)		Questions and House/School Dust Scenario (N=107)	
PC#[b]	**Dimension Description**	**% variability explained**	**Dimension Description**	**% variability explained**
1	Pesticide sprayed in house and rooms sprayed	17.7	Pesticide sprayed in house and rooms sprayed	13.7
2	Child working in field	7.4	School and school dust measurements	8.8
3	Distance from home to agricultural field	4.9	Child working in field	5.8
4	Relationship to fields where pesticides sprayed	4.2	House dust measurements - OPs	4.3
5	Additional adults at home and working with pesticides	3.6	Grade, age, school dust sum and school dust permethrins	3.9
6	Sources of drinking water	3.6	Sources of drinking water	3.6
7	Number and age of people in household	3.1	Additional adults at home and working with pesticides	3.1
8	Pesticide sprayed outside home	3.0	Relationship to fields where pesticides sprayed	3.0
9	Mother's occupation	2.9	Distance from home to agricultural field	2.9
10	Height and weight of principal participant	2.5	Household dust sum and household dust permethrins	2.6
	Total for top/first 10 PCs	53	Total for top/first 10 PCs	52
	Total for all 29 PCs[c]	86	Total for all 35 PCs[c]	89
	Number of variables included in PCA	67	Number of variables included in PCA	89

[a] Based on Varimax-rotated component matrix and absolute loadings values greater than or equal to 0.6.
[b] PC# = principal component number.
[c] Based on PCs with eigenvalues $\geq$ 0.7 (Jolliffe 1986).

4.3.2.4 Classification Analyses

The technique Classification and Regression Trees (CART) (Breiman 1984) was selected as the primary type of data mining analysis. Details of the technique can be found in Appendix G, section G.2.4.1. The principal participants included in these analyses was limited to 130 children, those in kindergarten or first grade, from the initial eight study schools, and with available and non-suspect urine measurement data. Twelve CART analyses were performed (Table 4.3.14). Six of the analyses were performed with the log of the molar-weighted sum of ethylated DAPs (LWETHSUM), and six were performed with the log of the molar-weighted sum of the methylated DAPs (LWMETHSM).

The six CART analyses performed for each DAP sum evaluated the predictors selected under, or relative effectiveness of, increasing levels of information and measurement collection. Three levels of information were analyzed: questions, questions and household dust measurements, and questions, household dust and school dust measurements. For each of the three levels, two sets of questions were analyzed to compare the question predictors selected or relative effectiveness of the questions. The smaller set (LTD) included questions considered the more likely predictors of exposure levels; the larger set included all of the questions from the study. The analysis results can be used to compare the effectiveness of the information levels as screening tools to help identify participants with higher exposure levels, based on whether predictors from the dust measurements are selected when questions are available. CART analyses can handle independent variables with missing values; thus, scenarios including school dust measurements did not have to be analyzed with a smaller number of cases as for the PCA (section 4.3.2.3).

Table 4.3.14 Cross-Reference for CART Analyses Performed on Yuma Study Data

	Predictors Included				
Dependent Variable[a]	**Question Group[b]**	**House Dust**	**School Dust**	**Summary Table**	**CART Details-- Figures in Appendix G**
LWETHSUM	ALL	No	No	G.3.4 [c]	G.2.1.a, G.2.1.b
LWETHSUM	LTD	No	No	G.3.4 [c]	G.2.2.a, G.2.2.b
LWETHSUM	ALL	Yes	No	G.3.4 [c]	G.2.3.a, G.2.3.b
LWETHSUM	LTD	Yes	No	G.3.4 [c]	G.2.4.a, G.2.4.b
LWETHSUM	ALL	Yes	Yes	G.3.4 [c]	G.2.5.a, G.2.5.b
LWETHSUM	LTD	Yes	Yes	G.3.4 [c]	G.2.6.a, G.2.6.b
LWMETHSM	ALL	No	No	G.3.5	G.2.7.a, G.2.7.b
LWMETHSM	LTD	No	No	G.3.5	G.2.8.a, G.2.8.b
LWMETHSM	ALL	Yes	No	G.3.5	G.2.9.a, G.2.9.b
LWMETHSM	LTD	Yes	No	G.3.5	G.2.10.a, G.2.10.b
LWMETHSM	ALL	Yes	Yes	G.3.5	G.2.11.a, G.2.11.b
LWMETHSM	LTD	Yes	Yes	G.3.5	G.2.12.a, G.2.12.b

[a] LWETHSUM is log (molar-weighted sum of ethylated DAPs adjusted for creatinine); LWMETHSM is log (molar-weighted sum of methylated DAPs adjusted for creatinine). See Appendix F for more details.
[b] ALL represents analyses with all 67 questions used (Table G.2.1). LTD represents analyses with 29 of the 67 questions considered to be more likely predictors.
[c] See also Tables G.3.4 and G.3.7 for comparisons of CART analyses with and without CHLDTM3.

For ease of presentation, these classifiers will be termed predictors, although these analyses are not performed with the intent of offering traditional predictive tools as in regression analysis. Instead CART is used as a tool to understand the factors and the interactions of the factors that may affect the exposure measurement levels found in the Yuma Study participants. A summary of the predictors selected by the CART analyses gives an overview of the questions or measurements that were found useful in differentiating the levels of pesticide exposure for children in the Yuma Study (Table 4.3.15).

Table 4.3.15 Categories of Selected Predictors[a] from CART Analyses of DAP Sums for Yuma Study Participant Children

LWETHSUM[b,c]	LWMETHSM[d]
Child's characteristics (weight, ethnicity)	Child's characteristics (height, weight)
Proximity to agricultural fields, spraying conditions	Proximity to agricultural fields, spraying conditions, child outside when fields sprayed
Child's time spent away from home	
Diet - local fruits/vegetables	
Pesticide use inside home	Pesticide use inside home, where in house child spends time
	Father's occupation
	Child's school
Household dust: OPs, permethrins, non-OPs	Household dust: non-OPs, permethrins
School dust: OPs	School dust: none

[a] Predictors selected for CART analyses across more than 50% of the scenarios.
[b] Log (molar-weighted sum of ethylated DAPs) - section F.3.2.
[c] Predictors based on CART analyses without CHLDTM3 (Table G.3.4)
[d] Log (molar-weighted sum of methylated DAPs) - section F.3.2

Several predictors are similar across the two DAP sums:
- child's characteristics
- proximity of home to agricultural fields
- pesticide use in the home
- permethrins (in house dust).

The ethylated sum levels consider the time spent at home, locally-grown fruits/vegetables in the diet, and OPs in house and school dust. The methylated sum levels also consider the father's occupation and time spent outside when the agricultural fields are sprayed. These results seem plausible given the differences in the DAP metabolites expected from pesticide use scenarios in residences and in agriculture.

Note that although the details of the CART analyses are presented in Appendix G, it is important to recognize that the CART analyses were performed on a maximum of 130 cases. This level of N, and the range of the DAP sum measurements used as the dependent or target variables, may make the subpopulations identified in the CART analyses less precise than needed for prediction. The best use of the CART results is as "indicators" of predictors that are more useful in differentiating the exposure levels. The CART tree allows the user to note the localized interactions (at each node's split) between predictors making up the higher or lower exposure level subpopulations, especially for the first few levels of each tree. When trying to sort through a large number of predictors, the ability to identify localized rather than global interactions in a data set is one advantage CART analysis provides over traditional regression analyses.

4.3.2.5 Comparison of Questionnaire Responses for High and Low Ends of Measurements

A non-statistical approach was implemented to identify any predictors that could differentiate between the high and low exposure levels based on the DAP urinary metabolites. In the previous analyses, CART and CDC (2002), the questionnaire responses, dust measurements, and urine measurements for all of the participant children were considered. Because the range of the distribution of the urine and dust measurement values is limited, it seemed reasonable to compare the information of participants from the extremes of the available distribution. Thus, approximately 10% of the respondents from the low end of a specific distribution and approximately 10% of the respondents from the high end of the distribution were selected.

Twenty-one questions considered more likely to be predictors of a child's pesticide exposure level were identified. The weighted sum of the responses for each participant was created from 18 of the questions where the weight was added to the sum if the response indicated a potential exposure to pesticides. Table G.3.5 in Appendix G shows the questions used in the exposure weighted sum, and the amounts added to the sum based on the responses. The values of this weighted sum and the responses to the 18 individual questions (and to school, grade, and number of rooms treated) were compared between the high- and low-end values of each measurement sum to determine if any patterns in the responses were evident.

Table 4.3.16 Results from Non-statistical Comparison of Questionnaire Responses Between High and Low Ends of Measurement Sum Distributions

Measurement Sum[a]	Questions[b] Differentiating Between the High and Low Measurement Groups
WETHSUM + WMETHSUM	EXPOSURE SUM [d], FARFIELD [c], WHNCHMO[d, e], WHEEL [d], DADCON2 [d], MOMCON2 [c]
WOPSUM	SCHOOL, HOWCHEMO [d, e], FARFIELD [d], CLOSEAPP [d, e], WHEEL [d], CHLDTM7 [d], WHENFILD [d], CHLDFLD [d]
WDUSTSUM	SCHOOL, NRMSRYD [c], HOWCHEMO [d, e], OFTCHEMI [c], FARFIELD [d], WHNCHMO [d,e], WHEEL [d], SPRAYFLD [d], DADCON2 [c], MOMCON2 [d]

[a] See Appendix F for description of sums. Exposure sum is created using weighting scheme in Table G.3.5.
[b] See Table 3.5 for abbreviated description of question variables.
[c] Some difference ($\geq$ 15%) in responses between participants at both ends of measurement distribution was evident. Difference was in direction expected, that is, exposure to factor is associated with high-end measurement value.
[d] Some difference ($\geq$ 15%) in responses between participants at both ends of measurement distribution was evident. Difference was not in direction expected based on current knowledge; that is, t exposure to factor is associated with low-end measurement values.
[e] Some difference ($\geq$ 15%) in responses between participants at both ends of measurement distribution was evident. Difference is based on response (some exposure to factor) compared to non-response (Don't know, No response).

The questions that point to some differentiation of the exposure levels are reasonable; however, most of them show the difference to be in the direction opposite of what is expected based on current knowledge (Table 4.3.16). As in the results of CDC (2002), relationships with the responses are considered one question at a time. This view may hide interactions with other risk factors or it may point to other factors that have a related effect.

4.3.2.6 Summary of Results

The Yuma Study report (CDC 2002) looked at each question or dust measurement individually and included siblings as well as principal participants from 152 households using a general linear estimating model with repeated measures. The data mining approach used the questions and dust measurements simultaneously in CART analyses for only 130 principal participants in kindergarten and first grade. Given these and other differences, it may be useful to look with caution at a summary of the predictors selected under both approaches to evaluate the universal strength of the predictors for the ethylated DAP sum (Table 4.3.17) and the methylated DAP sum (Table 4.3.18). Only questions that could be applied, or were available for siblings as well as principal participants, were analyzed for the Yuma Study report (CDC 2002).

Table 4.3.17 Comparison of Selected Predictors from Yuma Study Report[a] and Data Mining Approach[b] for Sum of Ethylated DAPs[c]

Yuma Study Report	Data Mining Approach
Recent use of pesticides inside home	Recent use of pesticides inside home
Other adult in household working in agriculture	Child's characteristics (weight, ethnicity)
	Proximity to agricultural fields, spraying conditions
	Child's time spent away from home[d]
	Diet - local fruits/vegetables[d]
Household dust: OPs, permethrins, non-OPs	Household dust: OPs, permethrins, non-OPs
School dust: permethrins	School dust: OPs

[a] Based on Tables 4.3.4, 4.3.7, and 4.3.9 and molar-weighted sum of ethylated DAPs (adjusted for creatinine).
[b] Based on Table G.3.7 without CHLDTM3 and log (molar-weighted sum of ethylated DAPs-adjusted for creatinine).
[c] See definition in Appendix F.
[d] Question was not analyzed in CDC (2002).

Table 4.3.18 Comparison of Selected Predictors from Yuma Study Report[a] and Data Mining Approach[b] for Sum of Methylated DAPs[c]

Yuma Study Report	Data Mining Approach
No Questions	Child's characteristics (height, weight)
	Proximity to agricultural fields, spraying conditions
	Father's occupation
	Where in house child spends time[d]
	Child's school[d]
Household dust: diazinon, chlorpyrifos, permethrins, carbaryl	Household dust: diazinon, chlorpyrifos, permethrins
School dust: diazinon, permethrins,	School dust: none

[a] Based on Tables 4.3.4, 4.3.7, and 4.3.9 and molar-weighted sum of methylated DAPs (adjusted for creatinine).
[b] Based on Table G.3.5 and log (molar-weighted sum of methylated DAPs-adjusted for creatinine).
[c] See definition in Appendix F.
[d] Question was not analyzed in CDC (2002).

The analyses in the Yuma Study report (CDC 2002) consider questions and measurements that would apply as risk or exposure factors to the principal participants and the siblings. These factors may affect explanations of the variability of the pesticide metabolite levels across siblings within a household. The data mining approach focuses the analyses on a potentially less variable group of children. For the ethylated sum of DAPs, recent use of pesticides inside the home, and OPs, non-OPs, and permethrins in the household dust stand out as differentiators of children's exposure level across both approaches. For the methylated sum of DAPs, only permethrins and OPs in household dust were similar across both approaches, since no questions were found significant in the Yuma Study report.

4.4 Effective Predictors of Pesticide Exposure Levels

Two approaches were considered in this project: a literature review across multiple exposure studies and multiple metabolites, and a more in-depth review of one exposure study in Yuma County, Arizona (Yuma Study). Although the literature review covers many different studies, results about significant relationships may be more limited because of the focus of each publication reviewed. For the Yuma Study, all questions asked were available for analysis. Access to this level of detail for the studies in the literature review was not available, although it is likely that the statistically significant relationships are noted in the publications for questions asked in the study. Taking these differences into consideration, a summary of the broad categories of predictors selected as differentiators of children's pesticide exposure (based on urinary metabolites or environmental measurements) can be enumerated as in Table 4.4.1.

Table 4.4.1 Summary of Predictor Categories Selected as Useful in Differentiating Children's Pesticide Exposure Levels Across Two Approaches

Literature Review[a]	Yuma Study[b]
Residential pesticide use (inside and outside)	Residential pesticide use (inside)
Pets[c]	
Occupation of household members	Occupation of household members
Household location: urban vs non-urban[c]	
Child's characteristics (age, ethnicity, family income)	Child's characteristics (age, ethnicity, height, weight)
Child's behaviors (loading from hand wipe)[c]	
Dietary behaviors (organic food)[c]	Dietary behaviors (local fruits/vegetables)
Family hygiene practices	
Exposure levels of household members[c]	
Health status (diseases)[c]	
Smoking behavior	
(Proximity to agricultural fields)[d]	Proximity to agricultural fields, spraying conditions
	Where child spent time at home/not, or within home
Household dust	Household and school dust: permethrins, OPs and non-OPs

[a] Based on the "c" Tables 4.2.10.c - 4.2.20.c.
[b] Based on Tables 4.3.17 and 4.3.18.
[c] Small number of relationships using these questions categories.
[d] Proximity to agricultural fields for the literature review was related to dust measurements only.

It would therefore appear that residential use of pesticides, the occupation of household members, certain demographic characteristics of the children, dietary behaviors, and proximity to agricultural spraying are the strongest predictors of exposure. Household dust levels are also predictive of exposures in some cases. Future studies should focus on more accurate questionnaire information, and more complete urine sample collection to improve the likelihood of identifying key risk or exposure factors for children's pesticide exposure.

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