**Appendix C (The IRB-approved Protocol)**

# An EPA Pilot Study Evaluating Personal, Housing, and Community Factors Influencing Children's Potential Exposures to Indoor Contaminants at Various Lifestages – Research Protocol

Research Protocol revised in response to CDC IT Security review and CDC IRB review– December 3, 2014

United States Environmental Protection Agency, Office of Research and Development, National Exposure Research Laboratory and National Risk Management Research Laboratory, Research Triangle Park, NC

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# 1.0 INTRODUCTION

## 1.1 Rationale

The mission of the U.S. Environmental Protection Agency (EPA) is to protect public health and safeguard the environment. The EPA Office of Research and Development's (ORD) Sustainable and Healthy Communities (SHC) Research Program is designed to help decision makers implement environmental management in ways that increase sustainable benefits, such as reducing or eliminating indoor exposures to pollutants from building materials, insecticides, or chemicals found in consumer products. Research conducted in the Enhancing Children's Health project in the SHC program (SHC project 2.2.2) develops the information and methods that decision makers need to assess how the natural and built environments affect children's health and well-being, including asthma, obesity, and neurocognitive development.

Additionally, EPA ORD's Chemical Safety for Sustainability (CSS) Research Program is developing tools that will use systems approaches to advance the understanding of the links between exposures to chemicals and mechanisms of toxicity that lead to the development of disease. More than 80,000 chemicals are currently listed or registered for use in the U.S. under EPA authorities and at least a thousand more are introduced every year. Many of these chemicals have not been thoroughly evaluated for their potential risks to human health, wildlife and the environment, particularly throughout their life cycle. As a result, important aspects of chemical safety are not adequately understood, including the contribution of chemical exposures to the overall disease burden for susceptible populations. CSS research will dramatically increase the efficiency and speed of chemical evaluations, and will allow EPA to evaluate potential effects of chemical exposures on critical lifestages, such as the embryo and childhood, and other susceptibility factors, including genetics and co-existing diseases.

This EPA pilot study add-on to the Green Housing Study aims to support the needs of both ORD national research programs by addressing how young children's exposures to various indoor pollutants (both chemical and biological agents) change as a result of building renovation-based interventions, potentially affecting their asthma morbidity. In addition to supporting EPA research programs, this pilot study will provide additional information on chemical exposures and children's interactions with their environments to enhance ongoing research in the Green Housing Study's evaluation of green housing and impacts on childhood asthma. Additionally, this pilot study will provide an opportunity to evaluate sample collection methods and novel approaches to capture information (time activity information, consumer product use information) that may significantly decrease the burden hours for study participants in future study sites of the Green Housing Study.

The EPA pilot study add-on will apply to the 3$^{rd}$ study site of the Green Housing Study (New Orleans). It will be integrated into the regularly-scheduled activities of the Green Housing Study for approximately 12 months of data collection.

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1.2 CDC/HUD's The Green Housing Study

The Green Housing Study is a collaborative effort between the U.S. Department of Housing and Urban Development (HUD) and the Centers for Disease Control and Prevention (CDC). Three main goals of the Green Housing Study are to: 1) compare levels of certain chemical and biological agents and non-chemical stressors in green versus traditional, multi-family, low-income housing; 2) ascertain differences in the health of the residents in these homes; and 3) assess the economic impacts of the "greening" of housing—particularly those related to health. These goals will be accomplished in ongoing building renovation programs sponsored by HUD. Green housing includes strategies to reduce exposure to environmental contaminants, including but not limited to the use of integrated pest management practices, the use of low/no volatile organic compound (VOC) materials (e.g., paints, carpets), and improved insulation and ventilation practices. Briefly, both the green-renovated and comparison (no renovation) homes will be from the same housing development or neighborhood to ensure homogeneity with regard to housing type and other socioeconomic factors. Changes in environmental measurements (pesticides, VOCs, particulate matter [i.e., PM2.5 and 1.0], indoor allergens, and fungi) over a 1-year post-renovation period will be compared to pre-renovation measurements, such that each home's measurements will be compared with its own baseline measurements. This study design enables both a pre- and post-renovation comparison as well as a comparison between green-renovated and control homes in order to detect differences in exposure levels and asthma outcomes. Residents will participate for 1 month prior to renovation, the time required for renovation of their home, and 12 months after completion of the renovation. The duration of participation for residents of comparison homes is the same. The detailed study design and all documents associated with the Green Housing Study can be downloaded from the Reginfo.gov website: http://www.reginfo.gov/public/do/PRAViewDocument?ref_nbr=201107-0920-004. Basic information on the Green Housing Study is included in Appendix A.

A brief discussion of the CDC/HUD Green Housing Study specific aims and hypotheses are discussed in the following paragraphs. The specific aims of the study are to:

1) Conduct an exposure assessment of chemical and biological contaminants, pesticides, VOCs, fungi, indoor allergens (in terms of variety and concentration) in green versus comparison housing.
    a) The Green Housing Study will measure interior levels of pesticides in surface wipe samples; fungi and indoor allergens in dust samples; and VOCs in air samples.
    b) The Green Housing Study will compare levels of biomarkers of VOCs and pesticides (in terms of variety and concentration) from the participating residents of green and comparison housing.
2) Examine the relationship between living in green versus comparison housing and asthma morbidity (e.g., symptoms, emergency department (ED) visits, use of medications, lost school/work days) of children with doctor-diagnosed asthma (ages 7-12 years). The study will adjust for allergic sensitization and environmental tobacco smoke (ETS).

The hypotheses of the CDC/HUD Green Housing Study are:

1) Green housing utilizes different strategies to reduce environmental contaminants. It is hypothesized that these strategies will lead to 1) lower levels of environmental contaminants

compared with those of comparison housing and 2) lower levels of related biomarkers in the residents of green versus comparison housing.

a. Integrated pest management (IPM) is a method to reduce pests such as cockroaches and mice by eliminating entry points in the home and harborage areas.
    i. It is hypothesized that IPM will result in lower cockroach and mouse allergen levels while at the same time lowering the concentrations and array of pesticides in the green versus comparison homes.
    ii. It is hypothesized that concentrations of pesticide metabolites in urine of children living in green housing will be lower than those living in comparison homes.
b. The use of low VOC paints, carpeting, and other building materials contain lower concentrations of aldehydes, ketones, and alcohols.
    i. It is hypothesized that the levels of VOCs will be lower at baseline in green-renovated versus comparison homes.
    ii. It is hypothesized that concentrations of VOCs in urine of children with asthma (ages 7-12 years) living in green housing will be lower than those living in comparison homes.
c. Insulation can reduce sources of moisture, specifically condensation. It is hypothesized that green housing will have more and possibly better insulation (e.g., higher R-value) than comparison housing. It is hypothesized that insulation (e.g., dual-paned windows, insulated cold water pipes, and rigid insulation above concrete floors and in exterior walls) will result in lower concentrations of dust mites (and therefore their allergens) and fungi.
d. Another aspect of green housing is improved ventilation which can reduce moisture and decrease indoor concentrations of VOCs. For example, improved exterior wall insulation can reduce condensation and a properly-sized and maintained central heating, ventilating, and air-conditioning unit (HVAC) can help buildings keep dry and at the same time, exhaust environmental contaminants to the outside.
    i. It is hypothesized that green housing will have a higher percentage of units with the recommended air exchange rates than comparison housing.
    ii. It is hypothesized that green housing units will have lower VOCs than comparison homes.
    iii. It is hypothesized that green housing units will have lower levels of fungi and dust mite allergens than comparison homes.

2) If irritants and allergens are lower in green versus comparison housing, residents of green housing should experience decreased asthma morbidity. It is hypothesized that children with asthma (ages 7-12 years) in green housing will have lower asthma morbidity, adjusting for environmental tobacco smoke (ETS) exposure.

In partnership with HUD and CDC, EPA will leverage this opportunity to collect additional multimedia measurements and questionnaire data from the index children actively participating in the Green Housing Study and a sibling(s) in order to characterize personal, housing, and community factors influencing children's potential exposures to indoor contaminants at various lifestages. Additionally, by recruiting sibling(s) of the index children, we will examine how

lifestage affects children's exposures when children have the potential to be exposed to the same chemicals in consumer products found in their environment.

1.3 Background

Childhood is a sequence of lifestages where physiology, anatomy, and behavior characterize identifiable periods of development in successive stages for each individual. Children's physiological characteristics may influence their exposures to chemical and biological agents found in their everyday environment either by affecting their rate of contact with various media or altering the exposure-uptake relationship. Children's behaviors and the ways they interact with their environment may also influence their exposures to chemical and biological agents in their environment. Developmental stage, physical activity, diet and eating habits, sex, socioeconomic status, and race/ethnicity are factors that have been identified as potentially impacting a child's exposure. Understanding exposure factors is essential in evaluating a child's aggregate and cumulative exposure to environmental chemicals and biological agents and identifying which factors most influence a child's potential exposure. It is important to have current information on children's exposure factors, especially activity pattern information and ingestion rates, since these exposure factors often drive modeled exposure estimates.

In addition to a child's physiological and behavioral characteristics, the physico-chemical characteristics of a chemical, activities in the household, and housing factors may also influence a child's potential exposure to various chemicals. For example, housing factors associated with an asthma diagnosis include ETS, presence of dampness/mold, roaches, and furry pets (Freeman et al., 2003). Synthetic chemicals have been incorporated into virtually all consumer products and consumers may be exposed to a myriad of these manufactured chemicals through direct or indirect contact with products (Rudel et al., 2003; Schettler, 2006; Weschler, 2009; Dodson et al., 2012). There is growing recognition that the most important pathways of exposure involve direct interaction with chemicals originating from consumer products (Jayjock et al., 2009). Direct exposure among users may be accompanied by indirect exposure among non-users, including children (Rudel and Perovich, 2009). For example, although children typically do not directly use shower mildew removing products, they still may be exposed to the chemicals in those products as they translocate through air and partition into dust. Additionally, many chemicals in personal care and cleaning products are suspected endocrine disrupting chemicals or are associated with asthma (Dodson et al., 2012).

Consumer products, household furnishings and appliances, and building materials can contribute to chemical exposures in residential environments. Given the large number of products and their chemical constituents, relatively little information is available about exposures correlated with the presence or use of these products in the home. Recent studies have investigated usage patterns of household and personal care products (Wu et al., 2010; Bennett et al., 2012) as well as chemical ingredients of these products, including chemicals not listed on product labels. While little information is readily available in the scientific literature on any difference in usage patterns of household cleaning and personal care products among minority or low income population groups, there exists a growing body of evidence of disparately high exposures to household item-related chemicals like phthalates and brominated flame retardants among low-income populations (Adamkiewicz et al., 2011; Quirós-Alcalá et al., 2011).

The relationship between housing type and characteristics and asthma-related symptoms may be affected by chemicals emitted from household and personal care products. As an example, it is reasonable to consider whether chemicals in these products, particularly triclosan, parabens, and other chemicals associated with allergic sensitization (Savage et al., 2012) may mask or otherwise distort the effects of building renovation-based interventions. Information from household and personal care product inventories combined with information on usage patterns is needed to examine the potential for effect modification.

Housing conditions, such as warm temperatures and excess moisture, as well as types of building materials, may also influence a child's potential exposure to various biological agents. Common indoor biocontaminants include mold, bacteria, viruses, dust mites, protozoa, and allergens (e.g., those from dust mites, cockroaches, rodents, pets). Under favorable environmental conditions (i.e., warm temperature and high humidity), some of these biocontaminants are able to grow and replicate on a variety of building materials and indoor surfaces. For example, mold exposures have been associated with a number of respiratory symptoms (Gorny, 2004; Fisk et al., 2007; Quansah et al., 2012). The Institute of Medicine Report *Damp Indoor Spaces and Health* (IOM, 2004) and the WHO guidelines for *Indoor Air Quality: Dampness and Mould* (WHO, 2009) found sufficient scientific evidence to conclude that mold exacerbates asthma. Epidemiological studies have associated mold with asthma, allergies, and /or sick building syndrome (Mendell et al., 2011). Animal studies using specific molds, such as *Aspergillus fumigatus*, *Penicillium chrysogenum*, and *Stachybotrys chartarum*, have demonstrated a cause-effect relationship between these molds, allergy and asthma-like syndrome (Viana et al., 2002; Chung et al., 2005, 2007, 2010; Pestka et al., 2008; Ward et al., 2008). Conversely, another study indicated that low fungal diversity in house dust is associated with childhood asthma development (Dannemiller et al., 2014).

In 2007, EPA, in conjunction with HUD, developed the Environmental Relative Moldiness Index (ERMI), a standardized assessment scale to quantify mold contamination (Vesper et al., 2007). The ERMI methodology classifies mold species from settled dust into two groups: 26 species related to water damage (group 1) and species primarily from the outdoor environment commonly found inside homes (including those without water damage) across the United States (group 2). The ERMI scale was used to evaluate mold exposures in about 200 homes in Cincinnati Ohio (Reponen et al., 2011). In this ten year prospective study of asthma development, researchers and physicians monitored the environment and health of infants until the age of seven years when a diagnosis of asthma was made (Reponen et al., 2011). The only exposure predictive of asthma development for these infants was living in high ERMI homes and the risk nearly doubled for each 10 units on the ERMI scale (Reponen et al., 2012). In another study, the ERMI values in post-Katrina water-damaged homes in New Orleans were correlated with the respiratory health of the children living in those homes (Vesper et al., 2013a). We found that the higher the ERMI values in the child's home (i.e., the greater the mold contamination) the poorer the child's lung function, based-on spirometry testing results.

Community exposure factors are defined as components of the natural and built environments (including non-chemical stressors) that influence children's health and well-being. The natural environment encompasses climate, weather, and natural resources that affect human survival and economic activity and includes all living and non-living things occurring naturally on Earth. The

built environment refers to the man-made surroundings that provide the setting for human activity, including but not limited to, buildings and infrastructure, land use, transportation, waste and materials management, water supply, energy needs, healthy food access, community gardens, walkability, and bikability. The natural and built environments affect health and well-being through the interactions that people have with their environment, including exposure to chemicals, activity patterns and active lifestyles, access to ecosystem goods and services (e.g., walking trails, parks, mountains, clean air and water), and access to other services perceived as important for a high quality of life.

Data are limited on the inter-relationships between exposure factors, housing factors, and community factors and their combined impact on children's exposures from chemical and biological agents in their indoor environment. Understanding how these factors affect asthma morbidity for children diagnosed with asthma is important in regards to prioritizing approaches to prevent childhood asthma. Additionally, data are limited on how chemical and biological agents found in the indoor residential environment may change as a result of green renovation. There are few studies in the literature that compare chemical and biological agents pre/post-renovation when green and traditional housing are considered.

Even though dust is routinely collected in observational exposure measurement studies, its usefulness as an exposure metric and relationship to other environmental measurements have not been clearly demonstrated, particularly for consumer products. Dust is ubiquitous and found in all locations where a child might spend time including homes, day care centers, and schools. Although dust is varied in composition, its physical and chemical characteristics allow chemicals to sorb to particles. Research findings suggest that dust may be an important exposure metric for understanding children's exposures because dust serves as both a sink for chemical residues found in a child's daily environment and a source of potential exposure. Children's exposure to dust comes through incidental ingestion, inhalation of dust that becomes airborne, and through dermal contact. The analysis of dust for chemicals associated with consumer products may inform children's aggregate and cumulative exposures and improve our understanding of source strengths and movement within our living environments.

Likewise settled dust is an excellent source for mold spores and its metabolites (Iossifova et al., 2007; Vesper et al., 2007). Using culture-independent studies, Vesper et al. (2006a, b; 2013b) analyzed DNA extracted from settled dust samples utilizing mold specific quantitative polymerase chain reaction (MSQPCR). The ERMI showed that specific mold populations were associated with asthma in water damaged homes (Reponen et al., 2012). It was demonstrated that culture-independent studies of dust samples are a very useful molecular tool for analyzing the DNA of fungal/mold populations in diverse indoor environments.

Another approach to collect dust samples for fungal population analysis is electrostatic dust collection (EDC). The EDC is a relatively simple method for collection of settled dust that does not require assembly of air sampling equipment. It consists of four electrostatic cloths mounted in a 40 cm × 30 cm plastic folder that is exposed to the air for several days. Recent studies have shown that the EDC method strongly correlates with vacuum dust samples in yielding high levels of culturable fungi and endotoxin (Frankel et al., 2012; Noss et al., 2008). Likewise, a strong correlation of EDC dust samples and vacuum samples with airborne dust has also been shown

(Frankel et al., 2012). Evaluation of EDC dust samples for fungal DNA analysis using the most current molecular technologies will provide an exposure metric for understanding which fungal populations may be associated with asthma in children. High-throughput DNA sequencing (HTS) technologies provide the opportunity to holistically explore and identify indoor fungal population diversity (Adams et al., 2013; Dannemiller et al., 2013). In addition, the metagenomic data generated from the DNA of EDC dust samples can be used to identify genes and functions that are overrepresented among the fungal biota with particular attention to the gene expression associated with mycotoxin synthesis. Although over 450 mycotoxins of mold have adverse health effects, all mycotoxins are secondary byproducts, and it is quite plausible that previously unknown mycotoxins exist if the substrate supporting growth changes (Nielsen et al., 1999; Andersen et al., 2002; Jarvis and Miller, 2005).

## 2.0 EPA PILOT STUDY ADD-ON OVERVIEW AND OBJECTIVES

### 2.1 Overview

This EPA pilot study will be conducted in homes recruited to participate in the Green Housing Study at the third study site (New Orleans). The Green Housing Study is a pre/post renovation study where participants participate for one month prior to renovation, the time required for renovation of their home, and 12 months post-renovation. The third study site location will be determined by CDC. In the third study site, 32 green intervention homes and 32 comparison homes will be included. Both the green-renovated and comparison homes will be from the same housing development or neighborhood to ensure homogeneity with regard to housing type and other socioeconomic factors. Changes in environmental measurements (pesticides, VOCs, particulate matter [PM2.5], indoor allergens, fungi) over the 1-year follow-up period will be compared, thus each home's follow-up measurements will be compared with its own baseline measurements. In total, the EPA pilot study add-on will include approximately 12 months of data collection.

### 2.2 Objectives

This EPA pilot study add-on directly supports the aims and hypotheses of the Green Housing Study since changes in asthma morbidity are the primary health outcomes of interest to CDC. Additionally, by partnering with CDC on the Green Housing Study, the EPA will collect information to further its research agenda addressing personal, housing, and community exposure factors, chemical exposures, and health in young children. Together, CDC and EPA can evaluate methods and approaches to enhance additional data collection at future study sites. By expanding the scope of the Green Housing Study to include this EPA pilot study add-on, our understanding of children's exposures to chemical and non-chemical stressors and the inter-relationships between these stressors can be addressed. Furthermore, leveraging resources by partnering with CDC on an existing research study will efficiently utilize research funds.

To this end, several objectives will be evaluated in the EPA pilot study add-on to the third study site.

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Primary objectives:

1) Identify and characterize factors affecting children's exposures to chemical ingredients from consumer products found in their everyday environment in order to support the data and modeling needs of the exposure components of EPA's national research programs;

2) Evaluate the pilot study data metrics for incorporation in and enhancement of CDC's ability to understand the relationship between environmental exposures and asthma in green versus traditional low-income housing;

3) Compare multimedia measurements and survey data between pre- and post-renovation time points in green and traditional low-income housing to assess exposure related changes in the residence and participants due to renovation activities.

Objective 1 will examine how influential personal, housing, and community factors are in determining children's exposures. Results will be used to directly compare siblings and determine how personal and housing factors vary. For siblings living in the same household, we hypothesize that shared exposures to housing and community factors both before and after building renovation will be similar. Thus, we hypothesize that personal exposure factors, including activities and behaviors, will most influence exposure to chemical and biological agents found in their indoor environment. Furthermore, the variability in personal exposure factors will be a function of age, lifestage, and health status (asthma versus no asthma). We can use this information to parameterize, refine, and evaluate exposure and dose models for consumer product active ingredients. Because of the lack of data on personal, housing, and community factors from the same cohort, it is necessary to collect these data to evaluate this objective.

Objective 2 will evaluate the pilot study methods and approaches for measuring exposures to consumer product chemicals and identifying exposure factors. It will also establish suitability for incorporation in future Green Housing Study sites and for future research directions. Our data collection effort is intended to complement the multimedia measurements and information being collected by CDC in the Green Housing Study. Methods found to be suitable in the pilot study will allow EPA and CDC to improve the evaluation of relationships between environmental exposures and asthma in the renovated and non-renovated homes.

Objective 3 will examine how exposure changes throughout the renovation period and differences between renovated and non-renovated homes. All multimedia measurements, activity pattern information, and survey data will be used to evaluate changes in exposure over time. Results will be used to directly compare various time points for exposure. We hypothesize that the types of chemicals the children are exposed to during the post-renovation period are significantly different than the chemicals the children are exposed to prior to renovation, and that differences between renovated and non-renovated homes will be observed.

Secondary objectives:

4) Evaluate exposure to chemicals in household cleaning and personal care products as a modifying factor in interpreting the effectiveness of green housing renovations on reducing the incidence of asthma-like symptoms;

5) Examine the relationships between consumer products in a residence, environmental concentrations, and exposure to active ingredients found in consumer product chemicals to support development and evaluation of models for predicting exposure to these chemicals;

6) Measure biomarkers of consumer product chemicals for young children in conjunction with environmental measurements to evaluate exposure and dose models;

7) Assess rapid, low burden, low cost methods for charactering consumer product use in the residential environment to predict exposure to chemicals;

8) Use low burden techniques and survey instruments to collect current information on children's activities, locations, and dietary habits to support exposure models and databases;

9) Use settled dust to identify and classify indoor fungal populations and functions overrepresented among fungal biota;

10) Evaluate the feasibility of using a simplified mass balance approach to estimate chemical exposure and dose rates incorporating children's toenail clippings, other multimedia measurements, and activity information;

11) Examine the feasibility of obtaining extant community-level data and prepare draft approaches for using such data for children's community exposure factor assessment and multiple stressor effects on estimates of health risks.

To accomplish objective 4 we will collect information on the types of household cleaning and personal care products used inside the home as well as information on the duration and frequency of their use. We will examine the association between the primary risk factor (renovation status) and the outcome (symptom incidence) to evaluate possible modifying effects due to chemicals emitted from consumer products, controlling for medication use. We hypothesize that exposure to household cleaning and personal care products will change the relationship between incidence of asthma-like symptoms and renovations to green housing standards.

Objective 5 will support development and evaluation of models for predicting exposure to consumer product chemicals. Measurement and survey results will be analyzed for linkages to the potential for exposure.

To evaluate exposure and dose models, chemical concentrations (parent and metabolite(s)) need to be measured in both environmental and biological matrices in order to serve as data inputs. Select pesticides and their metabolites have been used to evaluate various exposure models (e.g.,

SHEDS-Multimedia); however, few model evaluations have been conducted for other chemical types. These models need to be evaluated for consumer product active ingredients because of their prevalence in the indoor environment and potential asthma morbidity in young children from potential exposures. Biomarker measurements will be collected in order to evaluate objective 6. Results from objective 2 will be employed to assist in these analyses.

To accomplish objective 7 we will evaluate a novel method for rapidly characterizing consumer product inventories in the residential environment. We hypothesize that pictures can be used to adequately capture information on consumer products being used in the home. The results from this effort will then be used to predict exposures to chemicals.

There is a lack of current information on children's activities, locations, and dietary habits, and objective 8 will generate such information. We hypothesize that children's activities, locations, and dietary habits are dependent on age, lifestage, and factors related to their home and community. In combination with multimedia measurements being collected in the Green Housing Study, results from this objective will be used to estimate aggregate and cumulative exposures.

Results from objective 9 will be used for the DNA analysis of mold from dust and measurements of the ERMI values at each time point. We hypothesize that the electrostatic dust collection method is adequate to collect enough dust for DNA analysis. From these electrostatically collected molds, DNA will be extracted and analyzed using HTS analysis. HTS technologies provide the opportunity to holistically explore and identify diverse indoor fungal populations. In addition, the metagenomic data generated from the DNA of dust samples will be used to identify genes and functions that are overrepresented among the fungal biota.

The data collected for objective 10 will be used to explore the feasibility of using a simplified mass balance approach to estimate chemical exposure and dose rates for very young children. The goal of this objective is to evaluate the relationship between toenail clippings, blood, feces, duplicate diet, and dust to determine the feasibility of using these multimedia measurements to estimate chemical exposure and dose rates for very young children in observational exposure measurement studies. Associations between potential sources, exposure pathways, and indoor/outdoor concentrations will be evaluated. We hypothesize that toenail clippings can be used as a surrogate for blood concentrations and linked with various environmental measurements to develop a new approach to estimate chemical exposure and dose rates. If proven feasible, this approach could be applied to future epidemiological studies to generate current data on chemical exposure and dose rates.

Analysis of data for objective 11 will be used to understand the feasibility of collecting extant data on community exposure factors and how these factors may be applicable to other types of exposures and outcomes.

2.3 Sample Size Considerations

The sample size for the EPA pilot study add-on is fixed and dependent on CDC's grantee's ability to recruit and retain participants. Using available chemical concentration data for limonene (Sarigiannis et al., 2011), we can estimate the effect sizes we can see given various sample sizes (assumptions: design effect = 2.0, statistical power = 0.8, alpha level = 0.05, correlation = 0.3).

Example: Limonene in air ($\mu g/m^3$)

If non-renovated homes have a mean concentration and standard deviation = $15.0 \pm 19.4$ $\mu g/m^3$, with a fixed sample size of n=35 participants in each group (renovated and non-renovated homes), we could see a minimum size difference of 11.9 $\mu g/m^3$.

2.4 Strengths and Limitations

There are several strengths to this EPA pilot study add-on, including, a large cohort of children; siblings; longitudinal design; opportunity to collect multimedia measurement information for consumer product active ingredients. Additionally, by collaborating on this study, EPA can wisely use its limited resources to collect non-chemical stressor information.

We recognize and acknowledge that there are also limitations to this EPA pilot study add-on. The biggest limitation is the sample size, which is fixed and dependent on CDC's grantee's ability to recruit and retain participants throughout the time period of the study. In the main Green Housing Study, n=64 children (ages 7-12 years) with asthma will be enrolled. Therefore, n=64 younger siblings (only one sibling per household) will be the maximum number that could be enrolled as part of the EPA pilot study add-on. The sample size of the younger siblings enrolled as part of the EPA pilot study add-on will influence the amount of data available for statistical analyses and thus influence the types of statistical analyses that may be conducted on the data.

2.5 Collaborations and Partnerships

CDC and HUD have a collaboration in place on the Green Housing Study. CDC and EPA have established an interagency agreement to complete the EPA pilot study add-on as part of the Green Housing Study third study site.

In partnership with HUD and CDC, EPA will leverage this opportunity to collect additional multimedia measurements and questionnaire data from the index children actively participating in the Green Housing Study and a sibling from each household in order to characterize personal, housing, and community factors influencing children's potential exposures to indoor contaminants at various lifestages.

The objectives of this EPA pilot study add-on support the research needs of the SHC and CSS national research programs, as well as the specific aims and hypotheses of the Green Housing Study. We believe additional opportunities for data analysis and collaboration will be identified.

Additional collaborations will be formed as they are identified to complete laboratory analyses or share data for future research efforts. A potential collaboration currently being considered is with Silent Spring Institute to share protocols and methods for collection and analysis of SVOCs in air. Another potential collaboration is with our colleagues in the Office of Research and Development, U.S. EPA who are interested in using the dust samples to enhance the EPA pilot study add-on objectives.

# 3.0 RESEARCH PROTOCOL

## 3.1 Overview

This EPA pilot study is an add-on to the third study site of the Green Housing Study and is designed to characterize and assess factors associated with children's exposures to chemical and biological agents to inform asthma morbidity. It will use the information already being collected in the Green Housing Study. In addition, it will collect additional environmental, personal, and biological samples and compile additional information on children's activities, residence, and community. The proposed data collection will improve the understanding of chemical exposure sources, routes, and pathways; further evaluate factors affecting children's contact with chemical residues found in their residential environments; identify non-chemical stressors to be considered for understanding young children's exposures to chemicals; and assess and improve predictive modeling approaches for young children's exposures to chemicals.

## 3.2 Study Location

The third study site will be determined by CDC based on site selection criteria detailed in their funding opportunity announcement. In the Green Housing Study third study site, the target sample size is 32 green renovated homes and 32 comparison homes. The target sample size for the EPA pilot study add-on is the same number of families as are recruited to participate in the Green Housing Study. Thus, n=64 younger siblings (only one sibling per household) will be the maximum number that could be enrolled as part of the EPA pilot study add-on. Participants in each family will include the index child and a sibling of the index child living in the same household, as well as the mother/caregiver. The index child is defined as the child recruited to participate in the Green Housing Study who ranges in age from 7-12 years with a doctor diagnosis of asthma. By including both the index child and a sibling, it is an opportunity to collect exposure information for two children living in the same household, allowing us to explore differences in exposure based on lifestage.

## 3.3 Sampling the Participants

### 3.3.1 Sample Selection and Eligibility

Eligibility for the EPA pilot study add-on will be limited to families who enroll to participate in the Green Housing Study. In addition to the index child, a sibling of the index child residing in the same home will be enrolled. The sibling age range of most interest is 0 – 3 years. However, since it may not be possible to recruit siblings in that age range from every family, eligibility will be based on the availability of the youngest sibling in the 0 to 12 year age range. An asthma

diagnosis is neither an eligibility requirement nor an exclusion criteria for a sibling of the index child. For the EPA pilot study add-on, the target sample size is the same number of siblings as index children that are recruited to participate in the Green Housing Study (n=64) , resulting in a sibling group in each family.

3.3.2 Participant Recruitment

As families are recruited into the Green Housing Study, they will also be considered for participation in the EPA pilot study add-on. Recruitment for the EPA pilot study add-on will only be performed in families enrolled in the Green Housing Study. The original/main Green Housing Study only recruits children with asthma (ages 7-12 years). However, the EPA pilot study add-on will also enroll eligible younger siblings (one per household) up to a maximum n=64, although it is not expected that every household will have a younger sibling.

Participating families will be recruited into the EPA pilot study add-on in the following preferential order:
1) Families with a sibling of the index child in the 0 to 3 year age range;
2) Families with a sibling of the index child in the 4 to 6 year age range;
3) Families with a sibling of the index child in the 7 to 12 year age range;
4) Families with no age-eligible siblings of the index child or those with age-eligible siblings that will not participate.

One sibling in each participating Green Housing Study family will be included, along with the index child and mother/caregiver. Recruitment efforts will focus on enrolling the youngest sibling. If the youngest sibling will not or cannot participate, and there are other siblings in the home, recruitment will proceed to enroll the youngest sibling for which there is agreement to participate (using the preferential order outlined above). If no age-eligible sibling can or will participate, recruitment will move to the next Green Housing Study family with eligible siblings.

3.4 Nested Study (n=9) to Evaluate a Simplified Mass Balance Approach to Estimate Chemical Exposure and Dose Rates for Young Children

Within the EPA pilot study add-on, an n=9 sub-study will be conducted to evaluate a simplified mass balance approach to estimate chemical exposure and dose rates for young children. To accomplish this, for a sibling who agrees to provide a blood sample, we will also collect duplicate diet, feces, and toenail clipping samples in order to use these matched samples to explore a simplified mass balance approach to estimate exposure and dose rates for young children.

A recent review of the literature shows very limited information on whether toenail clippings can be used to estimate young children's exposures to chemicals. While blood and feces can be used as integrated samples to estimate exposure, toenail clippings may also serve as an integrated sample to understand and evaluate what chemicals a young child is exposed to through diet and activity patterns. If a relationship between the blood, toenail clippings, and feces can be established, this may pave the way for a low cost, innovative, and non-invasive approach to estimate integrated exposures using toenail clippings.

# 4.0 MULTIMEDIA MEASUREMENT PLAN

## 4.1 Overview

The EPA pilot study add-on will collect additional multimedia samples and an additional questionnaire beyond those included in the Green Housing Study. A consumer product use inventory will also be administered and time location data will be collected for participating children. The EPA pilot study add-on sample and information collection will be implemented at all study visit time points for each family (baseline, baseline part 2, 6-month follow-up, 12-month follow-up) in the Green Housing Study. Tables 1 and 2 list the samples currently being collected in the Green Housing Study.

Table 1. Summary of clinical measurements currently being collected by CDC in the Green Housing Study.

| Factor | Index child (Age 7 – 12 years) |
|---|---|
| Blood[a] | ✓ |
| Urine[b] | ✓ |
| Pulmonary Function Test[b] | ✓ |
| Exhaled Nitric Oxide[b] | ✓ |
| Respiratory Symptoms Questionnaire[b,c] | ✓ |

[a]Sample collected at pre-renovation only; analytes listed in Appendix A.
[b]Samples collected at all time points; analytes listed in Appendix A.
[c]Questionnaire administered to mother/caregiver.

**Appendix C (The IRB-approved Protocol)**

Table 2. Summary of environmental measurements currently being collected by CDC in the Green Housing Study[a].

| Type of Assessment | Baseline | Baseline part 2 (after renovation is completed) | 6-Month Follow-Up | 12-Month Follow-Up |
|---|---|---|---|---|
| Allergens | ✓ | ✓ | ✓ | ✓ |
| Fungi | ✓ | ✓ | ✓ | ✓ |
| Pesticides | ✓ | ✓ | ✓ | ✓ |
| VOCs | ✓ | ✓ | ✓ | ✓ |
| Particulate Matter ($PM_{2.5}$) | ✓ | ✓ | ✓ | ✓ |
| Temperature | ✓ | ✓ | ✓ | ✓ |
| Relative Humidity | ✓ | ✓ | ✓ | ✓ |
| Air Exchange Rate | ✓ | ✓ | ✓ | ✓ |

[a]More details on methodologies provided in Appendix A.

4.2 Field Measurement Protocol

The additional sample and information collection planned for the EPA pilot study add-on is summarized in Tables 3 and 4. Table 3 lists the questionnaire, inventory, and activity information and who will provide/complete the information. Table 4 lists the multimedia samples to be collected. Multimedia measurements collected for the EPA pilot study add-on include indoor air, house dust (technician and participant collected vacuum), surface dust, electrostatic dust collection, surface wipes, soil, hand wipes, socks, duplicate diet, urine, blood, toenail clippings, and feces. Table 5 summarizes the collection and analysis methods for the multimedia samples being collected in the EPA pilot study add-on to the Green Housing Study.

Table 3. Information collection summary for the EPA pilot study add-on to the Green Housing Study.

| Information Type | Index Child (Age 7 – 12 years) | Sibling (Age 0 – 12 years) | Residence (Mother/caregiver) | Field Study Technician |
|---|---|---|---|---|
| Location, Transportation, Activity, Diet, and Consumer Products Questionnaire[a] | ✓ | ✓ | | |
| Consumer Products Inventory | | | ✓ | ✓ |
| Housing and Community Information | | | | ✓ |
| Accelerometer | ✓ | ✓ | | |
| GPS information | ✓ | ✓ | | |

[a]To be administered to mother/caregiver as described in the Green Housing Study protocol.

**Appendix C (The IRB-approved Protocol)**

Table 4. Multimedia sample collection for the EPA pilot study add-on to the Green Housing Study.

| Sample | Residence | Index Child (Age 7 – 12) | Sibling (Age 0 – 12) |
|---|---|---|---|
| Indoor air (active and passive) | ✓ | | |
| House dust[a] (Technician and participant collected vacuum samples) | ✓ | | |
| Surface dust by Swiffer | ✓ | | |
| Electrostatic dust collection | ✓ | | |
| Surface wipe | ✓ | | |
| Soil | ✓ | | |
| Hand wipe | | ✓ | ✓ |
| Socks | | ✓ | ✓ |
| Duplicate diet[c] (n=9) | | ✓, Optional | ✓, Optional |
| Urine | | ✓[b] | ✓ |
| Blood[c] | | ✓[b] | ✓, Optional |
| Toenail clippings[c] | | ✓, Optional | ✓, Optional |
| Feces[c] | | ✓, Optional | ✓, Optional |

[a]In addition to samples already being collected for allergens and fungi as part of the Green Housing Study protocol.
[b]Aliquot from biological samples already collected or scheduled for collection as part of the Green Housing Study protocol.
[c]Samples must be matched to participant and home for collection and analysis.

**Appendix C (The IRB-approved Protocol)**

Table 5a. Summary of field collection protocols for the multimedia samples and information being collected in the EPA pilot study add-on to the Green Housing Study.

| Sample | Collection Method | Study Specific SOP Number |
|---|---|---|
| Indoor air (active) | Standard Operating Procedure (Sop) for Collection of Indoor Air Samples using Active Samplers | GHS-001 |
| Indoor air (passive) | SOP for Collection of Indoor Air Samples using Passive Samplers | GHS-002 |
| House dust (Technician collected vacuum samples) | SOP for Technician Collected House Dust Samples | GHS-003 |
| House dust (Participant collected vacuum samples) | SOP for Participant Collected House Dust Samples | GHS-004 |
| House dust (Electrostatic collection) | SOP for Collecting Swiffer™ Dust | GHS-005 |
| House dust (Swiffer collection) | SOP for Dust Collection using an Electrostatic Dust Fall Collector | GHS-006 |
| Surface wipe | SOP for Collection of Wipe Samples from Hard Surfaces | GHS-007 |
| Soil | SOP for the Collection of Soil Samples | GHS-008 |
| Hand wipe | SOP for Collection of Dermal Wipe Samples | GHS-009 |
| Socks | SOP for Collecting Sock Samples | GHS-010 |
| Duplicate diet | SOP for Collection of Duplicate Diet Samples | GHS-012 |
| Urine | SOP for Collection of Urine Samples; SOP for Collecting Diaper Samples for Urine Analysis | GHS-011, GHS-013 |
| Blood | SOP for Collecting Blood Samples | GHS-014 |
| Toenail clippings | SOP for Collecting Toenail Clippings for Metals Analysis | GHS-015 |
| Feces | SOP for Collecting Fecal Tissue | GHS-016 |
| Accelerometer | SOP for using Actical™ Activity Monitors in the EPA Pilot Study Add-On to the Green Housing Study (GHS) | GHS-017 |
| Global Positioning System | SOP FOR GPS Data Collection with the QSTARZ BT-Q1000XT GPS Travel Recorder | GHS-018 |
| Product Inventory | SOP for Collection of Household Cleaning Products and Personal Care Products Inventory | GHS-020 |
| Location, Transportation, Activity, Diet, Consumer Products, and Home Observation Questionnaire | SOP for Administering the Electronic Location, Transportation, Activity, Diet, Consumer Products, and Home Observation Questionnaire in the EPA/CDC Green Housing Study (GHS) Pilot | GHS-019 |

## Appendix C (The IRB-approved Protocol)

Table 5b. Summary of laboratory procedures (including both pre-sampling activities and post-sampling methods) for the multimedia samples being collected in the EPA pilot study add-on to the Green Housing Study.

| Sample | Sampling Media Preparation Method | Existing SOP | Chemical Analysis Methods[a] | Existing SOP |
|---|---|---|---|---|
| Indoor air (active) | NA (purchased pre-cleaned) | NA | Standard operating procedure for preparation of air samples collected on PUF plugs for GC/MS analysis | EMAB-SOP-001 |
| Indoor air (passive) | Cleaning and packaging of polyurethane foam (PUF) discs | EMAB-139.0 | Extraction pesticides and BFRs from PUF disks<br>PBDE in GC/MS/NCI | HEASD-XX.X<br><br>MDAB-79.0 |
| House dust (Technician collected vacuum samples) | NA | NA | Large-scale sieve shaker to sieve vacuum cleaner dust;<br>Processing house dust using glovebox;<br>PBDE in GC/MS/NCI;<br>PBDE in Dust;<br>Improved FTOHs house dust;<br>Improved PFAAs house dust | MDAB-83.0;<br>MDAB-89.2;<br>MDAB-79.0;<br>MDAB-81.0;<br>MDAB-21.0;<br>MDAB-XX.X |
| House dust (Participant collected vacuum samples) | NA | NA | See House dust (Technician collected vacuum samples)[b] | See above |
| House dust (Electrostatic collection) | Proper preparation and sterilization of electrostatic dust fall collector | Draft | Proper extraction of dust from an electrostatic dust fall collector | Draft |
| House dust (Swiffer collection) | NA | NA | | |
| Surface wipe | Cleaning and packaging of surface wipes | EMAB-138.0 | PBDE in GC/MS/NCI;<br>Analysis of cotton wipe samples for pyrethroids,<br>pyrethroid metabolites, OPs, BFRs, and Bisphenol A | MDAB-79.0;<br>EMAB-147.0 |
| Soil | NA | NA | Analysis of soil for selected insecticides in soil samples using a modified QuEChERS method | Draft |
| Hand wipe | Cleaning and packaging of surface wipes | EMAB-138.0 | PBDE in GC/MS/NCI; Analysis of cotton wipe samples for pyrethroids, pyrethroid metabolites, OPs, BFRs, and Bisphenol A | MDAB-79.0;<br>EMAB-147.0 |
| Socks | Cleaning and packaging of cotton garments | EMAB-140.0 | Preparation and analysis of cotton garment samples for pyrethroids, organophosphates, brominated flame retardants and pyrethroid metabolites | EMAB-150.0 |
| Duplicate diet | NA | NA | | |
| Urine | NA | NA | CDC methods | |
| Blood | NA | NA | CDC methods | |
| Toenail clippings | NA | NA | | |
| Feces | NA | NA | Modified feces digestion method based on Roberts et al. 2007 | |

[a]Chemical analysis methods listed will act as the basis for methods developed specifically for this study in order to analyze target analytes of interest.

NA=Not applicable

[b]The same methods will be used for technician and participant collected house dust.

4.3 Target Analytes

Table 6 lists the target analytes for the EPA pilot study add-on to the Green Housing Study. Including these chemical and biological agents complements the list of chemical and biological agents currently included in the Green Housing Study in order to better address the specific aims and hypotheses of the Green Housing Study and the objectives for the EPA pilot study add-on.

Myriad chemical and biological agents may be found in children's indoor environments. Several chemical and biological agents have been considered for inclusion in the EPA pilot study add-on because they are considered asthma triggers, exacerbate asthma symptoms, or otherwise impact asthma. Other criteria were also considered when developing the target analyte list. Scientific justifications for including specific chemical and biological agents are outlined in the following paragraphs.

Consumer product active ingredients: Consumer products, particularly personal care and household cleaning products, may contain an array of potentially hazardous chemicals to which children may have incidental exposure (Rudel and Perovich, 2009). Many of these chemicals are suspected endocrine disrupting chemicals or are associated with asthma (Dodson et al., 2012). Among the compounds targeted in the EPA pilot study add-on, linalool and limonene are common fragrance terpenes that auto-oxidize on air exposure to compounds that can cause contact allergy (Bråred Christensson et al., 2009), while triclosan and parabens have been found to be significantly associated with aeroallergen sensitization (Savage et al., 2012).

Metals: Children in the United States experience exposures to toxic metals like cadmium and arsenic from multiple sources and through multiple routes and pathways including inhalation, dietary intake, and ingestion of dust and soil. There is some evidence of adverse health effects resulting from *in utero* and early life exposures to cadmium and arsenic (Farzan et al., 2013; Rodríguez-Barranco et al., 2013; Schoeters et al., 2006). However, some factors affecting children's exposures to these metals – including relationships between children's activities and locations and non-dietary ingestion from dusts and soils – are not well understood. Uncertainties also remain in children's dust and soil intakes in their residential environment that can impact exposures to many different inorganic and organic pollutants. Measurement of some 'tracer' elements in residential dusts and soils (including aluminum, silicon, and titanium) in combination with activity information and biomarker measurements may help to better characterize dust and soil intake for children, leading to improved exposure factors for predicting children's environmental exposures. The collection of environmental and biomarker measurements proposed in the EPA pilot study add-on, along with collection of detailed time activity information, will assess methods and approaches for characterizing and predicting children's exposures and exposure factors for toxic metals and other pollutants in residential environments.

Pesticides: Children are exposed to pesticides in their residential environments through inhalation, dermal contact, dietary intake, and non-dietary ingestion of dusts and soil. It remains difficult to accurately predict children's pesticide exposures, and an important uncertainty is the relationship between children's activities and their contact rates with contaminated media. Pesticides included for the EPA pilot study add-on include chlorpyrifos, permethrin, fipronil, and

piperonyl butoxide (PBO). These compounds were selected as pesticide representatives because of their use and prevalence in indoor environments, toxicity characteristics, and a considerable body of scientific research and modeling at EPA.

Many pesticides persist in indoor environments because of low volatility and minimal UV light (Rudel et al., 2003). Chlorpyrifos is a broad range, non-systemic, chlorinated organophosphate insecticide that is a cholinesterase inhibitor (Zhao et al., 2006) and endocrine disruptor (Rudel et al., 2003). Even though sales of products containing chlorpyrifos for residential use were terminated at the end of 2001, it is still detected in indoor samples (Trunnelle et al., 2014). Permethrin is a pyrethroid insecticide that is currently registered for indoor use by both consumers and pest control professionals, for treatment of head lice and flea and tick control on pets. Permethrin has also been identified as an endocrine disruptor and is found in indoor dust (Mnif et al., 2011; Hwang et al., 2008). Fipronil is a phenylpyrazole insecticide used for controlling many pests (e.g., ants, termites, cockroaches) in the residential environment and direct application to pets for flea and tick control. Fipronil has been shown to inhibit thyroid hormone production (Mnif et al., 2011), has been classified by EPA as a possible human carcinogen, and is subject to future endocrine screening (U.S. EPA, 2011a). PBO is a chemical commonly used as a synergist in combination with pyrethroid insecticides and thus is a good marker of pyrethroid use (Stout et al., 2009). PBO has been classified by EPA as a possible human carcinogen and may be subject to future endocrine disruption screening (U.S. EPA, 2006). Unfortunately, the presence of pests, such as rat and cockroaches, are known to exacerbate asthma in children (Henderson et al., 2000; Perry et al., 2003). Several studies suggest that pesticide exposures may be an important cause in the occurrence and incidence of childhood asthma (Garry et al., 1994; Thrasher et al., 1993). Measurements in environmental and biological media and collection of detailed time activity information will provide information to better characterize important exposure factors that can be used to improve predictive exposure models and reduce our uncertainties in sources and pathways of children's exposures to pesticide chemicals.

Molds: The list of fungi (molds) in Table 6 includes, but is not limited to, fungi/molds identified in water-damaged homes. These were identified with culture-independent studies using quantitative PCR (Vesper et al., 2006a, b). The Environmental Relative Mold Index (ERMI) developed from the Vesper et al. (2007) research showed the fungi/molds in Table 6 associated with asthma in water-damaged homes. Previous research has demonstrated that the ERMI values in homes of infants and children are associated with asthma (Reponen et al., 2011, 2012; Vesper et al., 2013). For this study, we will evaluate the ERMI values pre/post-renovation, 6-months, and 12-months post renovation from the settled dust samples. In addition, we hypothesize that evaluating pre- and post-renovation dust samples for fungal DNA analysis with HTS technologies will provide the opportunity to holistically explore and identify more diverse indoor fungal populations. In addition, the metagenomic data generated from the DNA of dust samples will be used to identify genes and functions that are overrepresented among the fungal biota.

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Table 6. Targeted chemical and biological agents for the EPA pilot study add-on to the Green Housing Study.

| Target Compound Class | Target Chemical/Biological | Media | Biomarkers |
|---|---|---|---|
| **Consumer Product Active Ingredients** | Linalool | Indoor air, dust, surface wipe, urine, duplicate diet | -[a] |
| | Limonene | Indoor air, dust, surface wipe, urine, duplicate diet | -[a] |
| | Methyl paraben | Indoor air, dust, surface wipe, urine, duplicate diet | Methyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | Propyl paraben | Indoor air, dust, surface wipe, urine, duplicate diet | Propyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | Butyl paraben | Indoor air, dust, surface wipe, urine, duplicate diet | Butyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | Triclosan | Indoor air, dust, surface wipe, urine, duplicate diet | Triclosan conjugates, 2,4-dichlorophenol (2,4-DCP) |
| **Metals** | Aluminum | Dust, surface wipe, soil, hand wipe, urine, blood, toenail clippings, duplicate diet, feces | -[a] |
| | Arsenic | Dust, surface wipe, soil, hand wipe, urine, blood, toenail clippings, duplicate diet, feces | -[a] |
| | Cadmium | Dust, surface wipe, soil, hand wipe, urine, blood, toenail clippings, duplicate diet, feces | -[a] |
| | Silicon | Dust, surface wipe, soil, hand wipe, urine, blood, toenail clippings, duplicate diet, feces | -[a] |
| | Titanium | Dust, surface wipe, soil, hand wipe, urine, blood, toenail clippings, duplicate diet, feces | -[a] |
| **Pesticides** | Chlorpyrifos | Indoor air, dust, surface wipe, soil, hand wipe, socks, urine, blood, duplicate diet | DEP, DETP, 3,5,6-trichloropyridinol (TCPy) |
| | Permethrin | Indoor air, dust, surface wipe, soil, hand wipe, socks, urine, blood, duplicate diet | 3-PBA, 3-PBA glucuronide/glycine conjugates, *cis/trans*-DCCA |
| | Fipronil | Indoor air, dust, surface wipe, soil, hand wipe, socks, urine, blood, duplicate diet | Fipronil sulfone, desulfinyl fipronil, fipronil sulfide |

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| | | | |
|---|---|---|---|
| | Piperonyl butoxide (PBO) | Indoor air, dust, surface wipe, soil, hand wipe, socks, urine, blood, duplicate diet | -[a] |
| **Molds**[b] | *Aureobasidium pullulans* | Dust | Not applicable |
| | *Cladosporium sphaerospermum* | Dust | Not applicable |
| | *Penicillium crustosum* | Dust | Not applicable |
| | *Scopulariopsis brevicaulis* | Dust | Not applicable |
| | *Stachybotrys chartarum* | Dust | Not applicable |
| | *Trichoderma viride* | Dust | Not applicable |
| | *Wallemia sebi* | Dust | Not applicable |
| | *Alternaria alternata* | Dust | Not applicable |

[a]Denotes biomarker is parent compound.
[b]List includes, but is not limited to, molds found in the indoor environment and associated with asthma.

Should additional resources become available, additional chemicals may be analyzed in various media. This information is captured in Appendix B.

4.4 Multimedia Sampling Methods

Technicians for the Green Housing Study will visit homes during four visit periods (baseline, baseline part 2, 6-month follow-up, and 12-month follow-up). During each visit period, they will visit the home on Day 1 to collect samples/information and to deploy equipment, and return on Day 5 for sample and equipment collection. The EPA pilot study add-on will employ the same schedule to ensure that additional visits are unnecessary. Table 7 provides a timeline for the collection of additional information and samples to be collected for the EPA pilot study add-on during each visit period. The housing and community information, duplicate diet, toenail clippings, blood, and feces will only be collected at the baseline visit. The information/samples are listed in Table 7 in the order they are to be setup, discussed, or collected on a given visit day.

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Table 7. Timeline for collection of field samples.

| Information/Sample | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
|---|---|---|---|---|---|
| Indoor air – active | Setup | | | | Collect |
| Indoor air – passive | Setup | | | | Collect |
| Electrostatic dust collector (main play area, duplicate) | Setup | | | | Collect |
| Surface dust by Swiffer | | | | | Collect |
| Questionnaire | | | | | Collect |
| Consumer product inventory | Collect | | | | |
| Housing and community information[a] | Collect | | | | |
| Surface wipes (kitchen & bathroom, n=8) | Collect | | | | |
| Socks | Instructions[b] | Collect | | | Retrieve |
| Duplicate diet (n=9)[a,e] | Instructions[b] | Collect | | | Retrieve |
| GPS and accelerometer | Instructions[b] | Collect | Collect | Collect | Retrieve |
| Urine (toilet trained sibling)[c] | Instructions[b] | | Collect | Collect | Retrieve |
| Urine-diaper (non-toilet trained sibling)[c] | Instructions[b] | | Collect | Collect | Retrieve |
| Feces[a,e] | Instructions[b] | | Collect | | Retrieve |
| Toenail[a,e] | Collect | | | | |
| Blood[a,d,e] | Collect | | | | |
| Soil | Collect | | | | |
| Household vacuum bag | | | | | Collect (if available) |
| Technician vacuum sample | | | | | Collect |
| Hand wipe | | | | | Collect |

[a]These sample types will only be collected at the baseline visit.

[b]Instructions will be given to the caregiver for the use/collection of socks, duplicate diet, GPS, accelerometer, urine (cup or diaper), and feces on Day 1. During Days 1-5, the caregiver will complete the associated tasks to allow for retrieval of these data, items, and samples on Day 5.

[c]Only one type of urine sample will be collected for the sibling, depending on whether they are toilet trained. Diapers collected must contain only urine. First morning voids will be collected for toilet trained children on 2 days; first morning voids or convenience samples will be collected for non-toilet trained children on 2 days.

[d]Sibling blood samples are optional.

[e]Duplicate diet, feces, toenail clippings, and blood samples must be collected from the same participant (either the index child or sibling).

4.4.1 Environmental Samples

Additional environmental samples will be collected for analysis of chemicals of interest to EPA. Collection of field samples will be carried out by trained technicians using standardized protocols. A quality assurance project plan (QAPP) and standard operating procedures will be prepared and approved prior to collection of field samples. Field staff will be trained by CDC and EPA personnel. Environmental samples will include indoor air, house dust, soil, and surface wipes.

An indoor air sample will be collected from the main play area in the home. Both passive and active air sample collection will be used. The active air sampling approach will use low volume air samplers placed in a childproof, sound-proof housing and located in the child's play area. The pump flow rate will be sufficiently low to ensure that the pump can run for 5 consecutive days with minimum disruption to the study participants. A polyurethane foam (PUF) filled glass tube will be combined with a quartz or Teflon particle filter for collecting semi-volatile target analytes. Passive air collection will be performed by deploying a sorbent tube diffusion sampler in the child's play area. The passive sampler will collect volatile target analytes. The tube cap will be removed on the first day of sampling, and will be replaced on the return visit on Day 5.

House dust samples will be collected from a floor (preference: carpeted surface; alternate: hard surface) where the children may play or spend time. House dust will be collected using a forensic vacuum equipped with an in-line filter to collect and trap surface dislodgeable particles. The sampled area will be measured, marked, and recorded to ensure accurate documentation of amount of available dust for chemical and biological analyses. If available, field technicians will collect a participant's household vacuum cleaner bag. A swiffer settled dust collection protocol will also be used to collect settled dust from the tops of door jambs and bookcases. Dust samples will also be collected from the aforementioned areas using an electrostatic dust collector (EDC). Two EDCs will be placed horizontally at surfaces at least 1.5 meters above the floor and exposed for five days.

Surface wipe samples will be collected from impervious surfaces (e.g., hard floors, countertops) in a location where the children may spend time and/or locations where consumer products are stored and used (e.g., kitchen, bathroom). Multiple surface samples will be collected by wiping within a 144 square inch template placed on the impervious surface. Surface wipe samples will be gathered on cotton wipe media wetted with 6-mL of isopropanol.

Soil samples will be collected from an outdoor location in closest proximity to where the children spend time playing when outdoors. Soil samples will consist of scrapings collected to a depth of 2-3 inches using a pre-cleaned scoopula and placed into 8 oz. amber glass jars.

4.4.2 Personal Samples

Personal samples will include hand wipes, socks (to obtain surface-to-sock loadings), and a 24-hour duplicate diet. Hand wipes will be collected from the right and left hands of the sibling and index child. Cotton wipe media wetted with isopropanol will be used to wipe both hands.

The duplicate diet will be collected from only nine participants to minimize study burden. Preference will be given to homes where blood, toenail, and fecal samples are collected for the siblings. Duplicate diet will include both food and drink for a 24-hour period and analyzed for the metals listed in Table 6. Each participant will be provided with clean containers for the food and drink collection. Samples will be kept cool until picked up by the field technician.

4.4.3 Biological Samples

Urine and blood samples are being collected from the index children as part of the Green Housing Study protocol. An aliquot of these samples will be used to analyze for select biomarkers. Additional biological samples to be collected from the index child are toenail clippings. Urine, blood, toenail clipping, and fecal samples will be collected from the sibling(s) of the index child (Table 4). Urine samples will be collected as first morning voids. Diapers containing only urine will be collected for non-toilet trained siblings, with a preference for first morning voids, followed by a convenience sample. Collection of blood from siblings is an optional item for participants. Toenail clippings and feces will be collected by the mother/caregiver and analyzed for the metals listed in Table 6. In the event that a blood sample is not collected from the sibling, then every effort will be made to collect the toenail clipping and fecal samples from the index child in order to have a matched sample set for metal analysis (i.e., duplicate diet, blood, toenail clippings, feces).

4.4.4 Accelerometer and GPS

Activity and location data will be collected from both the index child and sibling on Days 2-4 of the study using minimally burdensome technologies, namely a waistband-mounted accelerometer-based activity monitor (Actical™; Philips Respironics, Bend, Oregon) and a Global Positioning System (GPS) Data Logger (model BT-Q1000XT; Qstarz International, Taipei, Taiwan). Field study technicians will prepare the devices for data collection and instruct participants on placement and use of the devices. Both devices will be worn by study participants during awake periods for all three days; the final day of data collection will correspond to the day covered by the EPA pilot study add-on questionnaire (collected on Day 5; questions are answered by participants for activities and locations for the preceding day, i.e., Day 4). The Actical™ requires no recharging during the data collection period; the BT-Q1000XT Data Logger will require recharging by the study participant's caregiver each evening. The devices will be collected by the field technician on Day 5 and the collected data downloaded and stored. Figure 1 shows the data flow for the accelerometer and GPS data.

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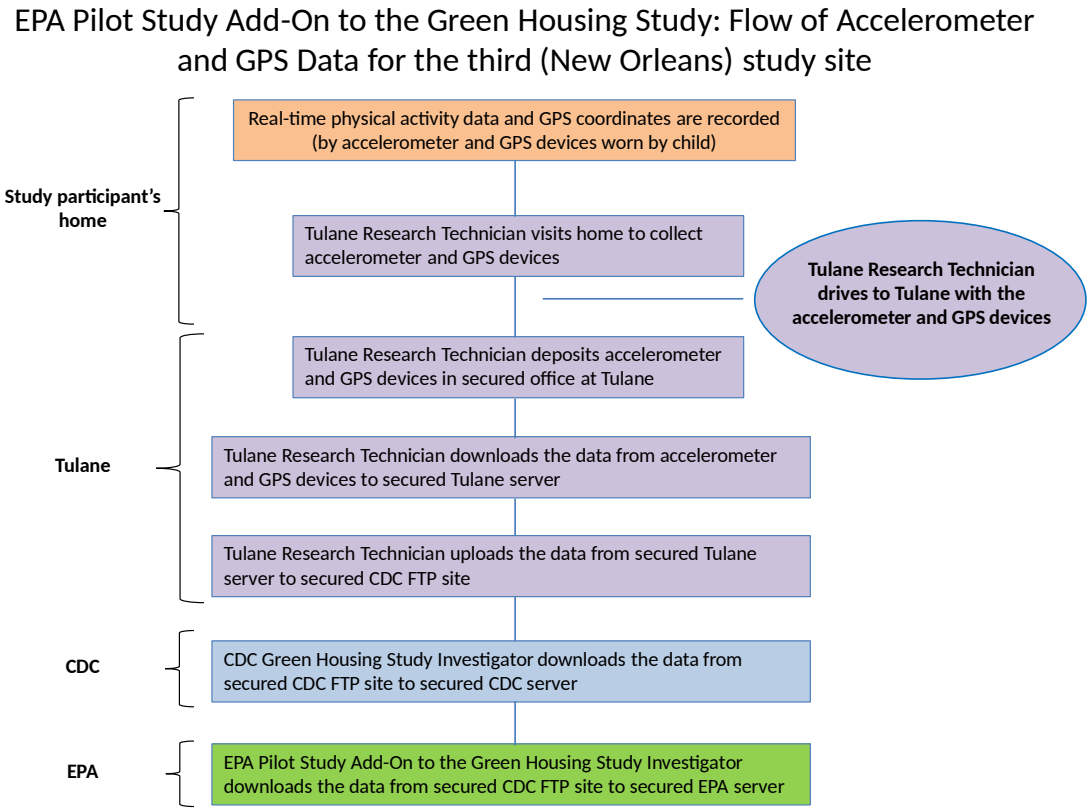
Figure 1.




4.4.5 Sample Processing and Shipment

Throughout the duration of the EPA pilot study add-on, chain of custody will be maintained for all samples collected in the field. Sample media will receive unique, individual labels and will be logged in the field to establish sample identification and chain of custody. All samples will be stored in a cooler at reduced temperatures during field collection and subsequently stored at -4ºC prior to shipping to the U.S. EPA laboratory in Research Triangle Park, NC. Upon receipt at the laboratory, the samples will be logged and stored at -20ºC or less.

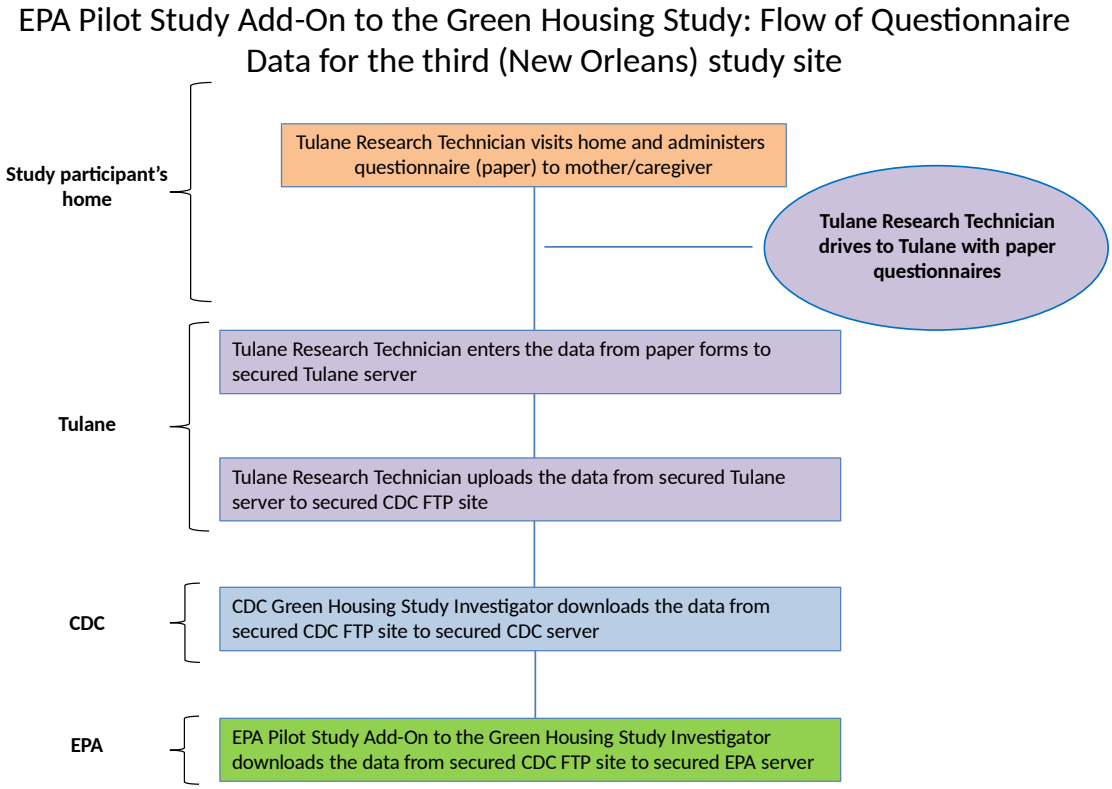
4.4.6 Sample Analysis

Organic chemical target analytes and biomarkers will be extracted from samples by one of several techniques such as pressurized fluid extraction, sonication, or Soxhlet. These compounds will be separated by gas or liquid chromatography and quantified using mass spectrometry. Metal target analytes will be extracted from samples by microwave digestion and analyzed using inductively coupled plasma mass spectrometry. Mold target analytes will be extracted using a liquid shaker technique and analyzed using mold specific quantitative polymerase chain reaction and high-throughput DNA sequencing.

4.5 Questionnaire

One questionnaire will query participants on location, transportation, activity, diet, and consumer products use and will be used by the field staff to record home observations (Appendix C). It will complement the questionnaires currently being used in the Green Housing Study and will be administered using a conventional pen and paper approach to the mother/caregiver for the index child and participating sibling(s). The questionnaire is primarily a recall questionnaire covering the activities of the index child and sibling(s) on the day prior to each field visit. Figure 2 shows the data flow for the questionnaire.

Figure 2.




Questions will gather information on the types of locations the children visited throughout the day, including residences, non-residential indoor environments (e.g., schools and stores), and outdoor environments. In order to reduce burden, questions will be asked about the 5 locations where each child spent the most total time. A series of transportation questions will also be asked related to how the children moved from one location to another to characterize time spent in vehicles or other near-road locations (e.g., street or bus stop). Questions will also ask about the types of activities performed in each location, with a primary focus on activities relevant to exposure to consumer products (e.g., bathing or grooming activities, chores, and contact with pets); however, other general categories of activities are included for estimating an overall level of energy expenditure for each child relevant to intake dose rates of indoor chemicals.

Additional questions are designed to address several aspects of the children's dietary habits related to chemical exposures, including information about the number of meals prepared in the home versus elsewhere, exposure-relevant food types (commodities/groups, e.g., dairy, green vegetables, meat), food forms (fresh versus processed), and sources of purchased groceries (e.g., supermarket versus farmer's market).

Finally, the questionnaire includes a number of questions designed to be used in conjunction with the data collected from the housing and community information questions. These include queries about the distance of all locations visited (e.g., parks) from the home, use of outdoor locations at home, the caregiver's perception of the general safety of their children in the locations visited, sleep quality of the child, and the use of public transportation.

The Green Housing Study questionnaires collect considerable information on housing factors. In order to better understand children's exposure factors, additional information will be collected, including technician observations of flooring and furnishings in each room, technician ratings of clutter and cleanliness, and information on the exterior area of the residential complex. The interior metrics will be used to assess the predictability of chemicals in house dust and as additional information for activity-exposure modeling. The exterior metrics (activity areas and surface types) will be used in assessments of child contact with soil, activity-exposure modeling, and the potential for residential track-in of measured chemicals.

Residential location information and selected activity information about the child's interaction with the larger community will be collected. Geospatial location of the residence will be used in the assessment of community attributes for domains that may be important for children's exposure to chemicals and for metrics of potentially important co-exposures and stressors; community-level domains may include pollutant sources such as roads and point sources, walkability, crime/violence, access to parks and food, neighborhood socioeconomic status, and other extant metrics depending on the study location. This information will not be collected through interaction with study participants – it will be obtained from extant data and geodata sources.

Information on usage frequency of household cleaning products and personal care products will be collected as part of the questionnaire. These questions are based on participant recall and cover typical cleaning and personal care activities carried out by any of the household residents. This section consists of three parts: (1) questions on the use of products in nine consumer product categories; (2) questions on specific types of household cleaning products; and (3) questions on specific types of personal care products.

4.6 Consumer Products Inventory

To generate an inventory of consumer products, the technician will photograph the locations where the participants indicate that household cleaning products and personal care products are stored. The technician will then send the pictures to EPA investigators (who will identify the products in the picture) using either email or multimedia messaging service. The technician will also inventory the products using a barcode scanner with memory. The image-based inventory (i.e., photograph) will be evaluated against the barcode-based inventory (i.e., technician collected

inventory) to assess collection accuracy. The barcode-based inventory will serve as the standard against which the image-based inventory will be evaluated. For quality control purposes, collection of the consumer product use frequency information may be administered more than once.

4.7 Community-Level Data

Field technicians will identify, obtain, and organize community-level data as part of a feasibility assessment with potential future application across multiple Green Housing Study sites. There are a number of community-level domains that may be relevant with regard to participant activity location information, pollutant sources, and socioeconomic factors that may be directly or indirectly associated with asthma. Previous research has shown associations between some community-level factors and asthma. There is little research to assess to what extent these community-level factors might influence or distort analyses of asthma outcomes based on measurements obtained in traditional and renovated housing. Some of the community-level domains that might involve chemical or non-chemical stressor exposures to children include: pollutant sources; demographic; socio-economic; transit/transportation; land use/built environment; playgrounds/greenspace; safety/social disorder; household; education/school; medical access; food access utilization.

The field technicians will work to identify extant sources for these data, with an emphasis on geocoded data. Data sources including census, state and municipal, public health, and extant GIS datasets will be considered. It is beyond the scope of this pilot study to perform study-initiated community data collections or to perform land-use regression types of pollutant modeling assessments, but those could be considered in future study activities.

# 5.0 DATA ANALYSIS PLAN

Our analysis approach will enable us to evaluate the objectives described in Section 2.0. Study participants will be characterized with regard to demographic variables such as age and gender as well as activity-related metrics from questionnaires and electronic devices. Housing and product information will be characterized based on questionnaire responses and technician information collection. Statistical analyses will be completed for target analytes and survey information at each study time point, as well as comparisons between time points and renovated/non-renovated homes. All media will be analyzed and compared between and among each media type. Cross-sectional, longitudinal, and pre/post renovation analyses will be conducted. Data quality (e.g., percent completion or detected, accuracy, precision) will be assessed to help make decisions on more complex statistical analyses that can be conducted with the available data.

Descriptive statistics, univariate analyses, and correlations will be employed to evaluate the pilot study data collected in the third study site. Descriptive statistics will be developed for all variables to be used in data analyses addressing the research objectives. Categorical variables will be summarized by frequencies, while continuous variables will be summarized by mean, standard deviation, median, and range. Environmental and biological measurement variables such as analyte concentrations in dust and urinary biomarker concentrations will be characterized by mean and standard deviation, median, range, appropriate distribution percentile values, and percent of measurements above the detection limit.

For detection limit censored data distributions, appropriate approaches for reducing bias in distributional parameter estimates will be considered (substitution, maximum-likelihood estimation, or beta-substitution, depending on the degree of censoring and sample sizes). Measurement distributions will be assessed for normality using the Shapiro-Wilks or other appropriate normality test. Depending on the distribution, measurement values may be log-transformed to compute geometric means and geometric standard deviations. Other types of transformations and/or non-parametric analysis methods will be considered if necessary.

Table 8 summarizes the data analysis plan, showing the relationship between the objective, data needed to evaluate the objective, and the proposed analysis approach.

As resources, time, and data suitability allow, additional analyses may be considered.

**Appendix C (The IRB-approved Protocol)**

Table 8. Summary of the data analysis plan

| Objective | Measurements Required | Proposed Analysis Approach |
|---|---|---|
| 1) Identify and characterize factors affecting children's exposures to chemical ingredients from consumer products found in their everyday environment in order to support the data and modeling needs of the exposure components of EPA's national research programs | Hand wipe, socks, house dust, air, soil, urine, blood measurements for target analytes; questionnaire and activity data | Descriptive and summary univariate statistics for measurement and survey data; correlation analyses within and between all collected data; geometric mean and standard deviation for target analytes to conduct t-tests of differences between sibling age groups; regression model analysis with target analyte measurements as outcome variables and product, activity, location, and housing variables as potential exposure factors |
| 2) Evaluate the pilot study data metrics for incorporation in and enhancement of CDC's ability to understand the relationship between environmental exposures and asthma in green versus traditional low-income housing | Survey responses from questionnaire; GPS; accelerometer data; housing data; multimedia measurement concentrations; QA/QC data for measurements and data collection; CDC measurement data | Data quality analyses such as precision, accuracy, range, % completion rate, % measureable, acceptability, compliance; descriptive statistics for measurement data; descriptive statistics for survey questions; correlations between survey responses on activity information and electronic information (GPS, accelerometer); correlations between EPA pilot study and CDC measurement data; assessment of impact of inclusion of EPA pilot study data in CDC asthma outcome models |

**Appendix C (The IRB-approved Protocol)**

| Objective | Measurements Required | Proposed Analysis Approach |
|---|---|---|
| 3) Compare multimedia measurements and survey data between pre- and post-renovation time points in green and traditional low-income housing to assess exposure-related changes in the residence and participants due to renovation activities | Chemical concentrations in available media (all chemicals, all media); mold information; activity information; all time points of data available for renovated and non-renovated homes; pre- and post-renovation information | Descriptive statistics; univariate statistics to compare chemical concentrations and mold at each time point and across renovated and non-renovated homes; correlations amongst chemicals and media; geometric mean and standard deviation for consumer product analytes in personal, residential, and biological samples by pre- and post-renovation time points; t-tests of differences between pre- and post-renovation time points; t-tests between siblings and pre- and post-renovation time points; non-parametric analysis of survey and activity response differences across time points and between renovated/non-renovated housing |
| 4) Evaluate exposure to chemicals in household cleaning and personal care products as a modifying factor in interpreting the effectiveness of green housing renovations on reducing the incidence of asthma-like symptoms | Number of asthma-like symptoms reported by each participant; renovation status; total dust loading/air concentrations of measured cleaning product ingredients | Multiple regression models to examine the association between the primary risk factor (renovation status) and the outcome (symptom incidence) before and after including possible modifying factors (chemical concentrations). If inclusion of the additional variable causes the association between the primary risk factor and the outcome to change by 10% or more, then the additional variable is a potential effect modifier. Care will also be taken to assess any contributions to the outcomes of interest that are due to changes in medication and exposure-related behaviors rather than renovation. |

**Appendix C (The IRB-approved Protocol)**

| Objective | Measurements Required | Proposed Analysis Approach |
|---|---|---|
| 5) Examine the relationships between consumer products in a residence, environmental concentrations, and exposure to active ingredients found in consumer product chemicals to support development and evaluation of models for predicting exposure to these chemicals | Household consumer product inventories, house dust, surface wipes, air, blood, urine concentrations | Quantification of relationships among media (dust, wipes, air) concentrations by chemical (correlations within and between subjects, descriptive statistics of ratio of air concentrations to surface concentrations); correlation between media (air and dust) concentrations and biomarker concentrations (within and between subjects by chemical); comparison of chemicals (individual or by class) in products found in the home with those found in dust and air (presence/absence) based on available databases of chemical ingredients; comparison of chemicals (individual or by class) in product categories reported as used in the home with those found in media (presence/absence, correlation of magnitude with reported use frequencies) based on available databases of chemical ingredients |
| 6) Measure biomarkers of consumer product chemicals for young children in conjunction with environmental measurements to evaluate exposure and dose models | House dust, air, duplicate diet, blood, urine concentrations; activity information; survey information | Descriptive statistics; correlation analyses; uni- and multi-variate analyses for biomarker measurements; model runs (e.g., SHEDS, PBPK model, PROcEED) for forward/reverse dosimetry; comparison (t-test, correlations) between measurements and model predictions |
| 7) Assess rapid, low burden, low cost methods for characterizing consumer product use in the residential environment to predict exposure to chemicals | Photographs of storage locations for household cleaning products and personal care products; barcode scanner inventory of products | EPA investigators will identify products in the photographs (blinded to scanner inventory). Image-based inventories will be evaluated against barcode-based inventories to assess collection accuracy (number of products correctly identified in photo divided by number in scanned inventory) |

**Appendix C (The IRB-approved Protocol)**

| Objective | Measurements Required | Proposed Analysis Approach |
|---|---|---|
| 8) Use low burden techniques and survey instruments to collect current information on children's activities, locations, and dietary habits to support exposure models and databases | Survey responses from questionnaire; GPS; accelerometer data | Descriptive statistics of reported time spent in microenvironments and activities; calculation of GPS-based time spent in microenvironments using MicroTrac model; quantitative comparison of questionnaire location results with GPS location results (paired t-test, correlations); quantification of accelerometer-based energy expenditures using accepted modeling methods; descriptive statistics of predicted energy expenditures by microenvironment and activity; coding of activity and location data in time-series format appropriate for exposure modeling |
| 9) Use settled dust to identify and classify indoor fungal populations and functions overrepresented among fungal biota | Fungal DNA extracted from dust samples | Qualitative analyses: HTS; identification and classification of indoor fungal population(s); identification of genes and functions overrepresented among the fungal biota<br>Quantitative analyses: ERMI; correlations; univariate and multivariate analyses; comparisons between pre- and post-renovation time points; renovated and non-renovated homes; comparison of collected dust types |
| 10) Evaluate the feasibility of using a simplified mass balance approach to estimate chemical exposure and dose rates incorporating children's toenail clippings, other multimedia measurements, and activity information | House dust, soil, hand wipe, surface wipe, duplicate diet, urine, blood, feces, toenail clipping concentrations | Descriptive statistics; univariate and multivariate analyses to compare chemical concentrations; correlations amongst chemicals and media; linear regression modeling incorporating multimedia measurements and survey information; geometric mean and standard deviation for elements measured in multimedia samples by pre- and post-renovation time points |

**Appendix C (The IRB-approved Protocol)**

| Objective | Measurements Required | Proposed Analysis Approach |
|---|---|---|
| 11) Examine the feasibility of obtaining extant community-level data and prepare draft approaches for using such data for children's community exposure factor assessment and multiple stressor effects on estimates of health risks | Domains of interest include: demographics, socio-economics, households, education/schools, safety/social disorder, birth outcomes, medical access, land use/built environment, playgrounds/greenspace, food access/utilization, transit/transportation, pollutant sources; indicators within each domain will be developed based on availability of extant data at the study location | Qualitative evaluation of success for identifying, accessing, and organizing extant community-level data; draft approaches for regression model analysis with personal and biomarker analyte concentrations and selected community domain indicators; draft approaches for hierarchical models to estimate individual and combined effects of community domain indicators and measured personal residential analytes on asthma-related morbidity measurements |

**Appendix C (The IRB-approved Protocol)**

**Objective 1: Identify and characterize factors affecting children's exposures to chemical ingredients from consumer products found in their everyday environment in order to support the data and modeling needs of the exposure components of EPA's national research programs**

The data analysis goal for objective 1 is to identify predictive factors associated with children's exposures to chemical and biological contaminants in their residential environments, with a focus on consumer product chemicals. Exposure factors of interest include housing characteristics, human activity, consumer product presence/use, and environmental contaminant concentrations and distributions. Exposure factor assessment will inform development and evaluation of exposure models for children. Identification of predictive factors that differ between green and traditional housing may also enhance CDC's ability to examine asthma outcomes in the Green Housing Study. Data analyses for this objective will be integrated with those for other objectives (particularly objectives 2, 4, 5, and 8).

Descriptive and summary univariate statistics will be compiled for measurement and survey data to identify variables with sufficient measurable results and variability to consider in factor analysis. Spearman/Pearson correlation analyses will be performed within and between all measurement data to elucidate relationships and associations. Geometric mean and geometric standard deviations will be calculated for target analytes by sibling/age groups. T-tests and/or F-tests of differences between measurement distributions across sibling/age group and other categorical product, housing, and activity factors will be calculated. In some cases, factor assessment by survey and activity data categories may require non-parametric tests. Where there are sufficient data, regression model analysis with target analyte measurements as outcome variables and product, activity, location, and housing variables as potential exposure factors will be constructed to examine relative contributions to variability in children's exposures. A specific goal of the analysis is to determine how, and to what extent, child activity factors might influence relationships between environmental contaminant levels and exposures as measured from hand wipe, sock, and biomarker concentrations.

**Objective 2: Evaluate the pilot study data metrics for incorporation in and enhancement of CDC's ability to understand the relationship between environmental exposures and asthma in green versus traditional low-income housing**

There are two elements for addressing Objective 2. First, the quality and suitability of measurement and survey data collected using the pilot study protocol will be evaluated. Second, for metrics found to be of adequate quality and suitability, EPA proposes to work with CDC to explore how incorporation of the additional exposure data may enhance the understanding of relationships between environmental exposures and asthma in renovated and traditional housing in the Green Housing Study.

Environmental, personal, and biological measurement data quality will be assessed by examining several factors including completeness, precision, accuracy, and percent measurable. Quality assurance objective criteria have been set for several factors: completeness (90%), precision (± 25%), and recovery (70 – 130%). Ideally, for a given analyte, the percentage of samples with analysis results greater than the limit of detection (or method limit of detection) will be >50% to facilitate estimation of relevant distributional parameters and to support data analyses including assessment of differences between groups, correlations, and linear regression modeling. Descriptive statistics for the measurement data will be used to document concentrations of target analytes found in the indoor environment. Comparisons to measurement data collected in other observational human exposure measurement studies will be completed.

Survey data include questionnaire responses, activity data, housing data, and product data. An important part of the pilot study is to assess the completeness and quality of survey data. To address the objectives in this research protocol, several approaches (e.g., barcode scanning, product photograph inventory, GPS, accelerometer) are being employed to collect personal, housing, and community exposure factor information for children. Results from traditional survey methods will be compared to collected data. For the questionnaire results, data quality analyses will be completed (as described in objective 8). There are several factors that will be examined to assess quality and suitability for use of the survey variables in exposure assessment. One goal is a >90% completeness rate for each survey variable. Comprehension and ability to provide requested information will be assessed through discussions with the field study team. Survey data will be examined to ensure that there exists a sufficiently diverse response range to be useful in distinguishing characteristics and activities where relevant in data analysis. The activity and location data collected using the questionnaire will be compared with the GPS and accelerometer data. Consumer product photographic inventory results will be compared to barcode scanning results for the products.

Following the initial step of assessing the measurement data quality and suitability for exposure assessment, EPA proposes to work collaboratively with CDC in exploring how the use of selected pilot study metrics may enhance the understanding of relationships between environmental exposures, activity, and asthma in the main Green Housing Study. The pilot study metrics, including the additional environmental measures and activity information, could be additional explanatory variables for asthma or could modify relationships for variables already collected in the main Green Housing Study. A goal of this evaluation is to identify which metrics may be candidates for incorporation into the full protocol at future Green Housing

Study sites. Pilot study metrics can be assessed directly for relationships with asthma metrics at this study site. They can also be incorporated into multivariate regression models. A key limitation will be the relatively small sample size at the single study site. While this exploratory analysis may be suggestive of relationships, there may not be sufficient statistical power for desired levels of confidence. However, this exploratory analysis may inform decision-making regarding incorporation of pilot metrics into future sites of the main Green Housing Study.

**Objective 3: Compare multimedia measurements and survey data between pre- and post-renovation time points in green and traditional low-income housing to assess exposure-related changes in the residence and participants due to renovation activities**

Indoor air, house dust, soil, hand wipes, socks, duplicate diet, and the biomarkers will be analyzed for the priority chemical analytes identified in Table 6. House dust will also be analyzed for the priority biological analytes identified in Table 6. Descriptive and univariate statistics will be used to describe the results for individual chemical/biological target analytes, media types, time points, and renovated/non-renovated housing. Analyses will also be conducted to describe the summarized results for each time point. The statistical analyses conducted to address objective 8 (children's activity information) will also be used for this objective.

When data from post-renovation time points become available, statistical analyses (t-tests, correlations) of pre- and post-renovation time points will be conducted for targeted chemicals, media type, and time point. Similar tests will be performed to assess differences between renovated and non-renovated homes. Analyses (t-tests, correlations) comparing siblings living in the same home will also be conducted. The multimedia measurements, activity information, and other extant data will be employed to estimate children's aggregate and cumulative exposures to selected target chemicals.

Using the systems approach for the holistic child framework developed at the EPA, we anticipate exploring the inter-relationships between chemical and non-chemical stressors (e.g., activity patterns, housing factors) and asthma to the extent that sample sizes allow.

**Objective 4: Evaluate exposure to chemicals in household cleaning and personal care products as a modifying factor in interpreting the effectiveness of green housing renovations on reducing the incidence of asthma-like symptoms**

Using the consumer product inventory obtained through objective 7, specific chemical ingredients will be gleaned from a publicly available household product ingredients database and from measurements reported by Dodson et al. (2012). Human exposure models will combine the usage frequency questionnaire responses with the inventories to predict anticipated residential concentrations. A select set of indicator chemicals will be used to evaluate this extrapolation through statistical analysis of the relationship between consumer products found in the home and measured chemical concentrations (objective 5). Multiple regression models will then be used to examine the association between the primary risk factor (renovation status) and the outcome (symptom incidence). If inclusion of a possible modifying variable (predicted or measured

chemical concentration) causes the association between the primary risk factor and the outcome to change by 10% or more, then the additional variable is identified as a potential effect modifier.

**Objective 5: Examine the relationships between consumer products in a residence, environmental concentrations, and exposure to active ingredients found in consumer product chemicals to support development and evaluation of models for predicting exposure to these chemicals**

For each residence, a chemical inventory of the products in the home will be performed (based on available databases of chemicals in products), and compared to media measurements (chemical presence/absence and group comparison of concentrations of chemicals in the consumer products versus other measured chemicals not found in consumer products). This information will be used in more complex analyses.

EPA has recently developed new methods for predicting exposure to chemicals in consumer products. These methods are implemented in the Stochastic Human Exposure and Dose-Simulation Model – High Throughput (SHEDS-HT) human exposure model (Isaacs et al., 2014). In order to accommodate high-throughput chemical assessments, SHEDS-Multimedia has been numerically and operationally modified to reduce user burden and increases run speed. The SHEDS-HT model uses a dynamic fugacity-based source-to-concentration module to estimate indoor concentrations by media (air, dust, and surfaces) for chemicals with indirect exposure scenarios, while direct scenarios (exposure during product use) are addressed via appropriate exposure equations. The concentration estimates, relevant exposure factors, exposure predictions, and human activity data are then used by the SHEDS-HT model to rapidly generate population distributions of potential exposures via dermal, non-dietary ingestion, and inhalation pathways. Due to the small sample size of the EPA pilot study add-on, direct comparison of predicted population SHEDS exposures and those measured in the pilot study may not be of use. However, the pilot study will provide a large number of matched product use, indoor media concentration, exposure (e.g., hand wipes), and biomarker measurements that could be used to evaluate individual algorithms or assumptions of the SHEDS-HT model. If the pilot study methods were incorporated into the main Green Housing Study, then direct comparisons between percentiles of predicted exposures and measured metrics could be performed (e.g., for groups with different consumer product use patterns).

SHEDS-HT is a mechanistic model that simulates the use of products in homes, transport of chemicals in these products into environmental media (air, dust, surfaces) in the residence, and human exposure as people contact the contaminated media. The model relies on algorithms that quantify the relationships between product use, media concentrations, and exposures. These relationships have been evaluated using available limited data (mainly for pesticides). The EPA pilot study add-on to the Green Housing Study will produce multimedia measurements for chemicals having properties much different than the chemicals previously used for model evaluation (i.e., pesticides). Examining these relationships in the EPA pilot study add-on to the Green Housing Study can validate the assumptions and results of the SHEDS-HT model for chemicals having a range of properties beyond those previously examined.

Quantification of relationship between the dust, surface, and air concentrations will be performed for all chemicals. Correlation coefficients will be calculated for multiple measurement days within single residences as well as across residences. Descriptive statistics of ratio of air concentrations to surface or dust concentrations will be calculated and compared to predicted chemical property-dependent ratios implemented in SHEDS-HT. Similar correlations between media (air, surface, dust) concentrations and biomarker concentrations (within- and between-participants by chemical) will be calculated in an attempt to determine a subset of chemicals for which chemical media concentrations are a useful surrogate for chemical exposures.

**Objective 6: Measure biomarkers of consumer product chemicals for young children in conjunction with environmental measurements to evaluate exposure and dose models**

Biomarkers will be analyzed in blood and urine samples for a complementary suite of chemicals to the target analytes investigated in the environmental samples. Descriptive and univariate statistics will describe measurements for the population, households, and individuals. Correlation and multivariate analyses/models will compare concentrations such as different biomarkers, different biological media, the same biomarker over time, and biomarkers to parents. This will summarize the data and provide the basis for determining which additional statistical analyses will be undertaken.

More complex analyses will be conducted for chemicals that have detections in at least one environmental and one biological media for at least one time point. Priority will be given to compounds that have existing PBPK models so that simple equations and/or default assumptions will not be required, or compounds that are indicated in asthma morbidity to support CDC study goals. As data permit, compounds with a range of persistence (environmental and biological) will be investigated by models.

Biomarker data can enhance exposure assessment through modeling in both a forward (exposure to dose) and reverse (dose to exposure) direction. Exposure and dose models such as NERL's SHEDS-Multimedia model and its variants use a probabilistic approach to predict the distribution of exposure and dose for a specified population. Inputs to the model include measurements (indoor air, house dust (preferential order: vacuum and surface wipe, socks, hand wipes)) and information collected from this study as primary inputs. These models use either a simple internal or a more complex PBPK model to predict the expected distribution of biomarker concentrations. The predicted distribution of concentrations will be compared (mean comparison by z-test, Chi-squared test for variance, ANOVA) with those measured to evaluate the use of such models and model parameters for young children.

Additionally, biomarker measurements will be analyzed in support of other study objectives. We will evaluate differences between case and control homes using ANOVA (objective 1). We will determine associations between a participant's biomarker concentrations before and after renovations using general linear and/or mixed models (objective 2). We will determine correlations between environmental and biomarker concentrations by chemical using Spearman and Pearson correlations (objective 5).

If samples sizes allow, the study participant data may be stratified (e.g., low/high concentrations, activity, age) to determine if the model can also predict differences between groups. If comparison of model predictions and measurements reveal large discrepancies, the Probabilistic Reverse dOsimetry Estimating Exposure Distribution (PROcEED) tool can be used to reveal exposure, data, or model gaps that require additional consideration. As resources, time, and data suitability allow, we will explore relationships for biomarker measurements between blood and urine and compare biomarkers indicating stress (cortisol, cytokines) with multimedia measurements, health status, and exposure factors (personal, housing, community). These relationships will be investigated using methods such as analysis of variance (ANOVA) and principal component analysis (PCA).

**Objective 7: Assess rapid, low burden, low cost methods for characterizing consumer product use in the residential environment to predict exposure to chemicals**

The information collected in the consumer products inventory and use frequency sections of the questionnaire will be analyzed to address research questions related to children's exposures to chemicals. EPA staff will work in teams to identify the products in the inventory pictures. The product types will then be entered into an electronic database for further electronic processing and analysis. Data analysis will consist of (1) comparison of photo-based inventory to barcode-based inventory and (2) evaluation of consistency between repeated product usage frequency surveys. Additionally, the chemical ingredients can be used to inform the laboratory analyses of the multimedia measurements (objective 5).

**Objective 8: Use low burden techniques and survey instruments to collect current information on children's activities, locations, and dietary habits to support exposure models and databases**

The information collected in the EPA pilot study add-on questionnaire will be analyzed to develop mean and variability metrics of exposure factors for the children's cohorts being studied, and to identify interactions or correlations among exposure factors that could be used to derive relationships for future assessments of children.

Activity and location data will be aggregated into an electronic database and further processed by EPA investigators into a format consistent with EPA's Consolidated Human Activity Database (CHAD; McCurdy et al., 2000, U.S. EPA, 2002). This format includes demographic, date, and housing information linked with a minute-by-minute diary of location and activity for the individual studied. It is anticipated that if the data quality from the questionnaires are adequate, these time activity data (de-identified) would be permanently entered in CHAD for use by EPA exposure models (and available to the public via download).

Understanding the type, magnitude, and variability of time spent in microenvironments across ages, geographic region, subculture, or socioeconomic status is critical in performing exposure assessments for different populations of children. Therefore, time spent in each microenvironment by each child will be summarized by standard methods (for example, Xue et al., 2004). Of specific interest will be differences in time spent in locations for children of different ages in the same household. Additionally, location information will be combined with

house dust loading measurements or personal samples in order to model children's soil and dust ingestion rates (objective 10). Finally, the interaction of time spent in different locations with housing and community factors such as crime rate, transportation options, and perception of children's safety will be quantified.

From the activity survey results, descriptive statistics of reported time spent in microenvironments and activities will be calculated. In addition, GPS-based time spent in microenvironments will be calculated using EPA's MicroTrac model (Breen et al., 2014). This model takes as input a GPS time-series and a general location of the participant's home and using a computational algorithm calculates time spent at home and in travel (in vehicles). The MicroTrac results will be compared with the survey results as in Breen et al. (2014). Differences among age groups, genders, and asthmatic/non-asthmatic children for both survey and GPS results will be quantified and tested using appropriate parametric or non-parametric techniques.

Children's activities are an important determinant of the types and amounts of chemicals encountered (McCurdy, 2000). Therefore, time spent in exposure-relevant activities (e.g., time spent with pet or exercising) will be characterized via standard methods (Xue et al., 2004). A primary analysis will evaluate age- and asthma-dependent differences in activity level in children living in the same household. The results from this analysis will aid in characterizing/elucidating the contributions of age, health, socioeconomic status, and other factors to describe the variability in activity levels. Similar to location, the interaction between housing and community factors (e.g., crime or noise pollution) and exposure relevant activities will be addressed. In addition, the location of high-dose rate activities (e.g., exercise) for these children will be compared to other, previously studied child cohorts to assess the influence of community or socioeconomic status-driven factors (such as distance from pollutant sources, or indoor versus outdoor exercise locations).

Exposure to chemical pollutants via dietary pathways is influenced by a large number of exposure factors related to food consumption habits. These exposure factors include habits or patterns related to: food types (food groups or agricultural commodities) (U.S. EPA, 2011b), food form such as fresh versus processed (Hamilton et al., 2004), home preparation of food (Melnyk et al., 2011), organic versus conventional, and source of food (supermarket, home grown, etc.) (U.S. EPA, 2011b). Questionnaire results relevant to these factors will be analyzed, summarized, and potentially compared with data from existing studies (USDA, a, b) or other available data to identify unique exposure-relevant dietary factors for these children. In addition, exposure factors developed from these questions will also be used to inform the modeling of intake of soil and dust via contamination of food prepared in the home. Finally, the relationships between these exposure factors and relevant housing and community factors (e.g., restaurant density, distance to food retail outlets) may be assessed.

**Appendix C (The IRB-approved Protocol)**

**Objective 9: Use settled dust to identify and classify indoor fungal populations and functions overrepresented among fungal biota**

One non-chemical stressor found in a home is mold. Molds are potential stressors because they produce allergens which have been shown to cause and or exacerbate allergies, diseases such as asthma, and affect immune system function. Because there are so many allergens, we measure the populations of molds as indicators of these agents.

We will use both the EDC method and the Swiffer settled dust collection protocol to evaluate the renovation process because both approaches provide insights into different timeframes and conditions for exposure. The EDC method is a measure of the mold cells in the air at a given time and the collection of settled dust is limited to short exposure time points. Additionally, the Swiffer settled dust collection protocol may represent what a child has been exposed to for a longer time period (many weeks to months depending on the frequency of house cleaning). Each method provides a different insight into the mold exposures in the home which is why both methods will be used and the results analyzed and compared.

DNA analysis of the dust collected using the Swiffer settled dust collection protocol will use quantitative PCR (polymerase chain reaction; qPCR). DNA analysis of the dust collected using the EDC method will be analyzed using high-throughput sequencing technology. Both approaches will be used to identify and classify indoor fungal populations and functions overrepresented among fungal biota.

Fungal DNA will be extracted from the EDC dust samples and analyzed using HTS analysis. This analysis will provide a holistic identification of the diverse indoor fungal population both pre/post renovation. This fungal DNA HTS analysis will provide an exposure metric for understanding which fungal populations are associated with asthma in children. In addition, the metagenomic data generated from the DNA of dust samples will be used to identify genes and functions that are overrepresented among the fungal biota. The pre/post renovation analysis will provide an exposure metric to understand the possible association, if any, between airborne mold and asthma in children.

The ERMI values from the renovated homes will be compared to the traditional homes at each time point using regression analysis. Comparisons between the settled dust and EDC dust will be conducted both pre/post renovation and green versus traditional housing using Pearson correlations. For each child, respiratory data (FEV1%) will be evaluated in relationship to the ERMI value in the home using Pearson correlation analysis. Univariate and multivariate regression analyses will be used to explore different stressors as well as the interactions between different stressors.

Mold information will also be incorporated into statistical analyses to explore relationships between ERMI values in the homes at different times with asthma-like symptoms. The differences in concentrations in the dust samples of individual mold species at each time point will be evaluated using the Wilcoxon rank sum test. Corrections for multiple comparisons will be made using the Holms-Bonferroni test. This test will allow us to determine which mold species are significantly reduced by the renovations. Other analyses will compare the type of

mold with presence/absence of asthma-like symptoms. This work will help inform sampling and sample size considerations in future study sites for the Green Housing Study and other studies.

**Objective 10: Evaluate the feasibility of using a simplified mass balance approach to estimate chemical exposure and dose rates incorporating children's toenail clippings, other multimedia measurements, and activity information**

The collection of toenail clippings is attractive because obtaining the sample is noninvasive and easily performed by the primary caregiver. Arsenic, cadmium, mercury, manganese, zinc and other elements may be sequestered in toenails and hair following environmental exposures and have utility in determining exposure and dose rates and serve as simple, low cost metrics to supplant other biomarkers, such as blood or urine, particularly for children. This objective will evaluate the relationship of toenail clippings with other environmental and biological measures and determine the feasibility of using toenail clippings to estimate chemical exposure and dose rates for very young children in observational exposure measurement studies. Associations and correlations between renovation activities, sources, exposure pathways, and indoor/outdoor concentrations will be evaluated. Descriptive, univariate and multivariate analyses will be conducted. Correlations (both Spearman and Pearson), linear regression modeling, and F-tests and t-tests will be conducted in order to evaluate relationships both within and between the measurement data to elucidate relationships and associations.

**Objective 11: Examine the feasibility of obtaining extant community-level data and prepare draft approaches for using such data for children's community exposure factor assessment and multiple stressors effects on estimates of health risks**

Environmental factors affecting children's health may not be limited to those in their immediate indoor residential space. Children may be exposed to environmental contaminants that originate elsewhere in their community. In addition, there may be non-chemical community-level stressors that result in joint effects with chemical stressors. For example, residential proximity to road traffic has been associated with asthma occurrence and exacerbations (Salam et al., 2008). Exposure to traffic pollutants may be mediated not only by children's activities, but also residential conditions. Other community factors, including community violence (Sternthal at al., 2010) and socio-environmental factors (Gupta et al., 2009) have been found to be associated with differences in asthma risk. Research is needed to better understand whether and how chemical exposures may interact with non-chemical stressors. Two approaches will be used to examine community-level effects or interactions. First, information will be collected about several aspects of the children's time, activity, and location with regard to their community and how it relates to their chemical exposures and health outcomes. Second, geospatial information will be used to examine several community-level domains for which extant data may be available in the city selected for the main study. These domains may include pollutant concentrations, pollutant sources, health, built environment, land use, neighborhood socio-economic status, crime, employment, education, food availability, and possibly other metrics where extant data suitable for geospatial analyses are available. When applied to only a single housing location, analyses will be limited to examining associations between children's interactions with the community and the child's biomarker and health measures. When applied to multiple housing locations,

additional analyses of relationships and interactions between community domain metrics, residential and personal chemical measures, and outcomes can be performed.

Draft approaches for regression model analysis with personal and biomarker analyte concentrations and selected community domain indicators will be examined. Of particular interest will be draft approaches utilizing regression and/or hierarchical models to estimate individual and combined effects of community domain indicators and measured personal or residential analytes on asthma-related morbidity. Such models could be considered for application across study sites in the Green Housing Study.

# 6.0 QUALITY ASSURANCE AND QUALITY CONTROL

A quality assurance project plan (QAPP) will be developed to specify and describe appropriate quality control and quality assurance measures and activities to ensure that data of known and high quality will be produced. Written sample collection and analysis standard operating procedures (SOPs) or research protocols will be included as part of the QAPP.

All sample collection media will be pre-cleaned or purchased as certifiably clean. Media will be evaluated prior to field deployment to ensure minimal background or interferences. Reference standards will be obtained from reputable and traceable sources. Spiking solutions will be prepared and applied to media following established operating procedures. Field and laboratory notebooks will be maintained as records to identify spike solution composition and concentrations and QC sample identifiers. Solvents used in the field for device cleaning or media preparation will be HPLC grade or better in purity. Field quality control samples will consist of blank, spike, and duplicate samples. Both blank and spike media will be transported to and from the field under similar conditions as field collected samples. Collocated samples will be collected where applicable. QC samples will constitute no less than 5% of all samples collected. Appropriate methods will be used to determine analytical and method limits of detection. If needed, blank and recovery correction will be used. Quality assurance review will be performed for all datasets.

Quality assurance procedures will be consistent with EPA guidelines:

- U.S. EPA. 2006. *EPA Requirements for Quality Assurance Project Plans*, QA/R-5, EPA/240/B 01/003, March 2006.
- U.S. EPA. 2007. *EPA Guidance for Preparing Standard Operating Procedures*, QA/G-6, EPA/600/B 07/001, April 2007.

**Appendix C (The IRB-approved Protocol)**

# 7.0 MANAGEMENT

Appendix D addresses the requirement of *Considerations for Protections of Human Subjects in the Study*.

## 7.1 Human Subjects

The study will be performed in accordance with human subject protections and procedures in place for the Green Housing Study.

## 7.2 CDC IRB/EPA HSRRO Approvals

The study protocol, consent and assent forms, and the questionnaire will be submitted for review and approval by the CDC Institutional Review Board (CDC IRB) responsible for human subject protections for the overall Green Housing Study. Following CDC IRB approval, the protocol and IRB materials will be submitted to the U.S. EPA Human Subjects Research Review Official (HSRRO) for review and approval. No study recruitment or data collection shall proceed until the CDC IRB and EPA HSRRO approvals are obtained.

## 7.3 Informed Consent and Assent

Informed consent is a critical element for protection of human research subjects. All mother/caregivers recruited into the Green Housing Study will provide informed consent for participation. Index children will provide their assent. A separate consent form will be used for mother/caregivers considering participation in the EPA pilot study add-on to the Green Housing Study. The CDC research team will discuss with the mother/caregiver, and the consent form will describe, the additional research elements that this study adds to the overall Green Housing Study. The study discussion and consent form will describe any potential risks for participation, which are anticipated to be minimal. The study will not provide any direct benefit to the participants. No monetary payments, gifts, or other remuneration will be provided for participation in the study beyond any included in the Green Housing Study. Participation in the study is voluntary. Participants can refuse to answer any question or decline to provide any sample or information and may withdraw from the study at any time. Decisions regarding participation or withdrawal from participation in the study will not affect their eligibility or participation in the larger Green Housing Study.

Only the mother/caregiver can provide consent for child participants under 18 years of age. A separate assent procedure will be used for children ages 7 to 12 years old. The CDC research team will describe the study sample and information collection procedures to the children, and children ages 7 to 12 years old will be asked to sign an assent form that explains the research procedures in simplified terms. Children may refuse to assent to participate and any who refuse will not be included in the study sample and information collection. For children under age 7, the consent of the mother/caregiver will be the basis for inclusion in the study research and separate assent from the child will not be obtained.

7.4 Confidentiality

Participant confidentiality will be maintained at all times and at all stages of research, reporting, and results dissemination. Limited personal identifying information shall be provided to U.S. EPA researchers by the CDC. All samples and information shall be coded with unique identification numbers, and U.S. EPA researchers will not have access to ID code translation keys. There may be occasions in which U.S. EPA researchers will need to visit study residences to evaluate or audit the implementation of research protocols. In these cases, limited personal identifying information will be shared only with the authorized person(s) making the residential visit and only for the purpose of that visit. The identifying information will not be retained by the U.S. EPA staff member(s) and will not be included in any study records maintained by the Agency. Photographs taken as part of the research protocol will be taken in a way so that they do not include images of study participants. Residence and participant geospatial information will be collected and used in analyses. Due to the nature of the housing, it is not anticipated that the information collected as nearest street intersection will allow the identification of individual participants.

7.5 Data Security

The U.S. EPA will maintain all study records in accordance with applicable policies and procedures necessary for FISMA compliance. Paper records will be stored in locked offices or locked file cabinets. Electronic records will only be stored on IT systems that are protected by the Agency's firewall and security systems. All electronic records will be backed-up on secure servers. The Agency will store personal identifying information in encrypted format on secure servers. Only U.S. EPA researchers working directly with the personal identifying information will be provided with the encryption key(s).

7.6 Staff Training

All U.S. EPA researchers will be certified as having relevant human subject protection training.

7.7 Data Reporting

The CDC will follow any existing Green Housing Study procedures for providing study results and information to study participants and the larger community. The U.S. EPA may use participant data and information in reports and/or publications, and may make research data and information available to the public. No identifying information will be included with or associated with any such public use of the data or information.

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# APPENDIX A

Parts A and B of the Green Housing Study OMB Submission

(OMB # 0920-0906)

**Appendix C (The IRB-approved Protocol)**

The Green Housing Study

Supporting Statement

(Part A)

October 20, 2011

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**Appendix C (The IRB-approved Protocol)**

A. JUSTIFICATION

A.1. Circumstances Making the Collection of Information Necessary

This ICR classification is New. This data collection uses Section 301 of the Public Health Service Act (42 U.S.C. 241) as the authorizing law (Appendix A).

Background

The efficacy of green building design features in reducing allergens and toxic substances within the home has been assumed based on conventional wisdom. A better understanding is needed of the extent to which green-built, low-income housing actually reduces exposures to these compounds when compared to standard-built, low-income housing. In addition, this study may provide insight into how specific green building practices (e.g., use of low chemical-emitting paints and carpets) may influence levels of substances in the home (such as volatile organic compounds (VOCs). A study investigating these topics would provide a solid foundation upon which to explore green affordable housing's potential to promote healthy homes principles. This investigation is consistent with the Centers for Disease Control and Prevention's (CDC) health protection research agenda, which calls for research to identify the major environmental causes of disease and disability and related risk factors. In addition, this study directly supports several of the United States Health and Human Services' (HHS) Healthy People 2010 objectives and the proposed 2020 objectives (proposed objectives available at www.healthypeople.gov/HP2020/Objectives/TopicAreas.aspx ):

Goal: Promote health for all through a healthy environment.

8-16 Indoor allergens
8-24 Exposure to pesticides
8-25 Exposure to heavy metals and other toxic chemicals
8-27 Monitoring environmentally related diseases

Goal: Promote respiratory health through better prevention, detection, treatment, and education efforts.

24-2 Hospitalizations for asthma
24-3 Hospital emergency department visits for asthma
24-4 Activity limitations
24-5 School or work days lost

Prior to this proposed study, there have been no multi-site studies of how green housing factors are associated with health effects such as asthma. Two main goals of this study are: 1) to compare levels of certain environmental chemical and biological agents in green vs. comparison, multi-family, low-income housing; and 2) to ascertain differences in the health of the residents in these homes. These goals will be accomplished in an ongoing building renovation programs including but not limited to public housing and "Mark-to-Market" (M2M), sponsored by United States Department of Housing and Urban Development (HUD). Thus, the residents of these homes are similar in terms of socioeconomic status. Briefly, the M2M program is a nationwide

initiative that encourages landlords of multi-family properties to use green building principles. In partnership with HUD, CDC will leverage this opportunity to collect survey and biomarker data from residents and to take environmental measurements in their homes. The results of this study will provide data that will allow CDC and HUD to identify housing factors that are not only energy-efficient, but have the potential to improve the health outcomes of one of the most sensitive populations, low-income children with asthma.

Many studies exist that examine the indoor environment in relation to health outcomes such as asthma. Table 1 lists contaminants in homes that have been shown to exacerbate respiratory symptoms.

Table 1. Contaminants in homes that are known to exacerbate respiratory symptoms.

| Factor | References |
|---|---|
| Moisture | Bornehag 2004, Franchi 2006, Gunnbjörnsdóttir 2006, Savilahti 2000, Skorge 2005 |
| Poor ventilation and heating | Franchi 2006 |
| Environmental tobacco smoke | Franchi 2006 |
| Wall-to-wall carpeting | Franchi 2006 |
| Pet allergens | Custovic 2003, Munir 2003, Skorge 2005 |
| Dust mites | Gotzsche 2004 |
| Cockroach allergens | Rosenstreich 1997 |
| Rodent allergens | Matsui 2006, Phipatanakul 2002 |
| Pesticides | Senthilselvan 1992 |
| Plastic materials | Jaakkola 2000 |
| Nitrogen dioxide | Zota 2005 |
| Combinations of the above | Salam 2004, Platts-Mills 2000, Sobottka 1996, Spengler 2004 |

Green building principles and indoor air quality:
Few studies have explored how green building practices affect indoor air quality (IAQ) and even fewer have examined how the health of occupants changed as a result of these practices. In Finland, IAQ and resident health were assessed in two buildings situated next to each other. One building had improved ventilation and policies against smoking and furred pets; the other had no intervention and served as the comparison. After one year, total VOCs were lower in the intervention vs. the comparison homes, and asthmatics in the intervention building reported improvements in respiratory symptoms (Tuomainen, Tuomainen, Liesivuori, & Pasanen, 2003). In a more recent study in the US, children who moved into asthma-friendly homes (e.g., improved ventilation, low VOC paint and cabinetry, improved insulation) and asthma education were compared to those who had received asthma education alone (Takaro et al., 2011). Exposures to mold, rodents, and moisture were reduced significantly in the intervention group and night-time awakening due to asthma was significantly different between the intervention and comparison group.

HUD Guidelines for Green Housing: In the HUD green renovation projects, several rehabilitation components could affect health. Some of these components are listed below. CDC and HUD will work together to document which of these occurred in the individual study homes.

-Window replacement
-Integrated pest management (IPM)* vs. traditional pest management
-Insulation
-Individual water heaters
-Heating and cooling equipment (appropriately sized)
-Central heating and cooling systems (appropriately sized and joints sealed in air distribution system)
-Cleaning products and materials
-Kitchen and bath exhaust fan
-Carbon monoxide alarms
-Smooth-surfaced floors
-Low VOC carpet
-Low or no VOC paint, primers, adhesives, caulk, and sealants
-Rubber walk-off mats
-Rubber stair tread
-Cementitious siding
-Changes to facilitate household waste recycling
-Green management of construction/rehabilitation debris
-Combined heat and power system
-Roofing replacement
-Landscaping replacement/modification
-Thermostat
-Air and thermal barriers

*Integrated Pest Management (IPM) – Comprehensive IPM involves reducing a variety of pests (e.g., rodents, cockroaches, termites, ants). Some IPM strategies are relatively easy to implement, while others are more difficult. For example, rodent- and cockroach-focused IPM can involve sealing food in containers, decreasing access to pet food sources, caulking cracks, and repairing holes in floors and walls. On the other hand, termite treatments can be more extensive. Optimally, IPM measures should be implemented with the advice of a professional trained in IPM. IPM has been shown to reduce cockroach and mouse allergen levels in homes (Arbes, Sever et al., 2003; Phipatanakul et al., 2004; Sever et al., 2007). The energy efficient design of green housing may incorporate many IPM principles, reducing the need for pesticides in these homes (Williams et al., 2006).

Cockroach allergens: Low-income inner city homes often have high levels of cockroach infestation. Both home and building-level characteristics can be related to high pest exposure (Chew et al., 2006; Rauh, Chew, & Garfinkel, 2002). Inner-city children were more likely to be allergic and exposed to high levels cockroach allergen than to dust mite or cat allergen (Rosenstreich et al., 1997). The children in the study who were allergic to cockroach allergen had three times the rate of hospitalizations and nearly twice as many unscheduled medical visits compared to non-allergic children or those allergic to dust mites or cat dander. Asthma severity has been linked to cockroach specific immunoglobulin E (IgE) in the sera of patients with mild, moderate, and severe asthma (Henderson, Ownby, Trumble, DerSimonian, & Kellner, 2000).

In 2000, the Institute of Medicine (IOM) concluded that:
1) There is sufficient evidence of a causal relationship between cockroach allergen exposure and exacerbation of asthma in sensitized individuals.
2) There is suggestive evidence of an association between cockroach allergen exposure and the development of asthma in preschool-age children.
3) There is insufficient information to determine whether or not associations exist between cockroach reduction, symptom improvement, and lung function in sensitized asthmatics (IOM, 2000).

Rodent allergens: The National Survey of Lead and Allergens in Housing estimated that detectable levels of mouse allergen existed in 82% of the nation's homes, and homes with low-income residents and older homes were likely to have increased concentrations of this allergen (Cohn, Arbes, Yin, Jaramillo, & Zeldin, 2004). Ninety-five percent of homes in the National Cooperative Inner-City Asthma Study contained Mus m 1 allergen in the settled dust (W. Phipatanakul, Eggleston, Wright, Wood, & Study, 2000a). The mouse allergen concentrations in many of these inner-city homes were similar to those found in animal facilities and were sufficiently high to elicit symptoms in sensitized individuals. However, the true source of a biologically relevant exposure in the home environment remains unknown. Many researchers have assumed that the bedroom would be the most significant source of exposure for many indoor allergens (Phipatanakul 2006). In New York, the mouse allergen levels in beds and kitchens were significantly correlated ($r= 0.63$, $p < 0.001$); however, kitchen levels tended to be higher ($p < 0.001$) and more variable (Chew, Perzanowski et al., 2003). Less is known about residential rat allergen exposure, although 33% of the homes of inner city children had detectable rat allergen, Rat n 1 (Perry, Matsui, Merriman, Duong, & Eggleston, 2003). The number of hospitalizations and unscheduled medical visits because of asthma were significantly higher in those children who were both exposed and sensitive to rat allergen.

Dust mite allergens: Most houses in temperate climates have several characteristics necessary for maintaining populations of mites. These include multiple nest sites for mites (e.g., carpets, upholstered furniture, and bedding); a food supply in the form of human skin scales; and temperature and humidity levels that are optimal for mite growth (IOM, 2000). Dust mites can produce an array of proteins, many of which have been shown to be allergenic to humans. Some of the most common taxa of dust mites include *Dermatophagoides farinae*, *D. pteronyssinus*, *Euroglyphus maynei* (Platts-Mills, Vervloet, Thomas, Aalberse, & Chapman, 1997; Voorhorst & Spieksma, 1969). In sensitized individuals, inhalation of Der p 1, an allergen from the dust mite *Dermatophagoides pteronyssinus*, causes an immediate drop in forced expiratory volume and may produce asthma-related late responses that persist for up to 2 weeks. In a study of 4 year olds, an independent effect of allergen sensitization on asthma was observed only with house dust mites, odds ratio 8.07 (95% CI 4.60–14.14) (Arshad, Tariq, Matthews, & Hakim, 2001). Other studies have demonstrated that moving asthmatic children and adults into mite-free environments was associated with improvement of asthma symptoms (Platts-Mills, Vaughan, Carter, & Woodfolk, 2000).

Allergens in the urban environment: At least two studies found that low-income African American children were neither sensitized nor exposed to high levels of cat allergen (Call, Smith, Morris, Chapman, & Platts-Mills, 1992; Huss et al., 2001). Several studies have demonstrated

that in homes where exposure to multiple allergens is likely, exposure to cockroach allergen or exposure to the combination of cockroach and dust mite allergen is the most significant predictor of sensitization and that these exposures are major risk factors for asthma (Alp, Yu, Grant, Rao, & Moy, 2001; Call et al., 1992; Gruchalla et al., 2005; Huss et al., 2001; Rosenstreich et al., 1997; Turyk et al., 2006). Dust mite concentrations greater than 2 µg/g have been associated with a greater risk of allergic sensitization (Sporik, Holgate, Platts-Mills, & Cogswell, 1990). Indoor allergen concentrations in excess of 8 U/g (cockroach) and 1.6 µg/g (mouse) have been associated with higher frequencies of medication use and medical provider visits (W. Phipatanakul, Eggleston, Wright, Wood, & Study, 2000b; Rosenstreich et al., 1997). Dust sample concentrations for rat allergen between 4 to 1413 ng/g were noted to be significantly higher in sensitized asthmatic children versus those without asthma (Perry et al., 2003). Average levels of allergens in the National Survey of Lead and Allergens in Housing were: 1.40 µg/g (dust mite), 0.292 – 1.376 U/g (cockroach), and 0.38 – 0.52 µg/g (mouse) (Arbes, Cohn et al., 2003; Cohn, Arbes, Jaramillo, Reid, & Zeldin, 2006; Cohn et al., 2004). Simultaneous exposure to fungi, indoor allergens (e.g., from cats, dogs, dust mites, cockroaches, mice and rats), and outdoor allergens (e.g., from grass, tree, and weed pollens) is common. Exacerbation of asthma in low-income populations is likely to be multifactorial, and no single exposure dominates (Brugge et al., 2003).

Because of different housing stock across the country, some home characteristics are not consistently associated with dust mite, mouse or cockroach allergen (Chew, Burge et al., 1998; Chew, Higgins et al., 1999; Phipatanakul, Eggleston et al., 2000; Rauh, Chew et al., 2002; Chew, Perzanowski et al., 2003; Cohn, Arbes et al., 2004; Matsui, Simons et al., 2005; Cho, Reponen et al., 2006). For example, the U.S. national housing survey which included information from buildings in 75 locations found that mouse allergen was higher in high-rise buildings (≥ 5 floors) compared to low-rise apartments (1-4 floors) (Cohn et al., 2004). This finding is not directly applicable to some cities such as New York where a majority of the housing in low-income neighborhoods is greater than 5 floors. In fact, shorter apartment buildings (i.e., fewer than 8 stories in New York) had 10-fold and 6.25-fold greater odds (compared with taller high-rise buildings) of having high mouse allergen levels in the kitchen and bed, respectively (Chew et al., 2003). This highlights the importance of considering the geographic factors that influence allergen levels within the home.

Fungi: There has been a substantial amount of research examining the impact of fungi and moisture on occupant health. Up to 40% of United States homes are reported to have problems with fungi (Brunekreef et al., 1989). Skin test results indicate that between 3 and 10% of persons worldwide demonstrate hypersensitivity to common airborne fungi (Horner, Helbling, Salvaggio, & Lehrer, 1995). Sensitization to allergens early in life increases the risk of developing asthma (Peat, Salome, & Woolcock, 1990). Specifically, sensitization to fungi is associated with the existence and severity of asthma (Bush & Prochnau, 2004; Jaakkola, Hwang, & Jaakkola, 2005; Maurya, Gugnani, Sarma, Madan, & Shah, 2005); inner-city children are especially affected (Crain et al., 2002; Kattan et al., 1997). Infants with a maternal history of asthma were significantly more likely to exhibit persistent cough and wheeze when exposed to increased concentrations of indoor fungi (Belanger et al., 2003; Gent et al., 2002). Furthermore, a Boston prospective birth cohort study found a significantly increased risk of developing lower respiratory tract illness among infants exposed to high indoor fungi levels (Stark, Burge, Ryan,

Milton, & Gold, 2003) and a greater risk of allergic sensitization by age 5 (Stark et al., 2005). The presence of a "mold odor" in a home, while controlling for confounding variables, has been shown to be an independent risk factor for the development of asthma with an incidence rate ratio of 2.4 (95% CI 1.1–5.6) (Jaakkola et al., 2005).

Homes with damp indoor spaces and high concentrations of fungi can aggravate pre-existing respiratory conditions such as asthma (IOM, 2004). The Inner-City Asthma study looked at homes demonstrating an increased concentration of fungi in the home compared to the outdoor air concentration measured on the same day (O'Connor et al., 2004). Residents of homes with higher concentrations of airborne fungi indoors than outdoors were significantly more likely to report dampness or leaks in any room, evidence of moisture and leaks, musty smell, and evidence of cockroaches. Modern building practices, such as increased use of synthetic building materials and inadequate ventilation or drainage, can promote fungal growth (NIH, 2005). Further research is needed regarding the efficacy of green building practices in preventing the growth of, or reducing the burden of, indoor fungi.

Volatile Organic Compounds (VOCs): A number of VOCs that can cause adverse respiratory effects are commonly found in the home environment. These include formaldehyde, benzene, toluene, xylene, ethylbenzene, and styrene, among others (IOM, 2000; Sunesson, Rosen, Stenberg, & Sjostrom, 2006). In 2000, the IOM concluded that there was insufficient evidence to determine whether or not an association exists between indoor residential VOC exposures and the development or exacerbation of asthma. The report recommends that indoor exposures to VOCs be limited where practical by source removal, source avoidance and increased ventilation. The IOM called for prospective cohort studies to characterize exposure (IOM, 2000).

Associations between VOCs and asthma: Following the IOM report, a few studies have provided preliminary evidence for an association between elevated VOC levels and adverse health effects, including asthma. Young Australian children with asthma were exposed to significantly higher VOC levels than controls (Rumchev, Spickett, Bulsara, Phillips, & Stick, 2004). Among the VOCs observed in this study; benzene, ethylbenzene, and toluene were most strongly associated with a primary diagnosis of asthma. The study also found that for each 10 $\mu g/m^3$ increase in concentration, the risk of having asthma increased by nearly two and three times for toluene and benzene respectively. In one study of asthmatic children living in public housing, 32% of samples collected hadbenzene levels that exceeded the cancer risk level, and 38% of samples had chloroform levels that exceeded the cancer risk level. Of all VOCs measured, toluene and 1,4-dichlorobenzene had the overall highest mean and maximum levels (Brugge et al., 2003) . A recent review article noted that although observational studies have identified an association between VOC and asthma indicators, further studies are needed to confirm this finding, characterize effect size, and determine the biologically relevant duration of exposure (Dales & Raizenne, 2004).

Pesticides: While health effects associated with pesticide exposure are myriad and range from mucus membrane irritation to neuropathies, cancer, and death (Amdur et al., 1991), we will focus on one main health outcome, asthma exacerbation. Similar to the case of VOCs, assessment of the biologically relevant time period of exposure can be difficult for pesticides. For example, a population-based school study in California found that children with pesticide

exposure in the first year of life were more likely to have early persistent wheezing than those not exposed during the first year of life (OR=3.6, 95%CI (1.6-8.1) (Salam, Li, Langholz, & Gilliland, 2004). In the same study, pesticide exposure at any other time (other than the first year of life) was negatively associated with early persistent wheezing (OR=0.7, 95%CI (0.3-2.0), but this did not reach statistical significance.

In the past, organochlorine, organophosphate, carbamate and pyrethroid pesticides could be found in most U. S. homes (Quandt et al., 2004). However, recent bans on residential use of chlorpyrifos (2002) and diazinon (2004) have led to lower exposures of these pesticides in the homes, particularly of inner-city apartments (Whyatt et al., 2004). Several housing characteristics have been found to predict indoor pesticide levels. For example, housing dilapidation has been associated with cockroach infestation, cockroach allergen and multiple pest eradication efforts (including use of pesticides) (Rauh et al., 2002). Many pesticides have low volatility and if not exposed to UV light, they can persist in indoor environments at high concentrations, although levels vary substantially depending on use level (Rudel, Camann, Spengler, Korn, & Brody, 2003). For these reasons, researchers who have studied pesticide exposure in children's homes, have concluded that household pesticides are best measured via dust sampling (Bradman et al., 2005).

Pesticides and asthma: There are considerable data indicating that dysregulation of both parasympathetic (cholinergic) and sympathetic autonomic control of airways, such as by pesticide exposure, may be important in the occurrence of asthma and its severity (P. J. Barnes, 1995). Dysregulation of parasympathetic function predicts the onset of wheezing in adults. (Sparrow, O'Connor, Basner, Rosner, & Weiss, 1993) Although there are few direct studies of the effects of organophosphate and carbamate pesticide exposure on asthma risk, farm workers' exposure to carbamate pesticides has been associated with the occurrence of asthma after adjustment for other relevant factors (Senthilselvan, McDuffie, & Dosman, 1992). Professional fumigators have an increased occurrence of allergy and asthma in parallel with a greater than 20% decrease in red blood cell levels of acetylcholinesterase (Garry, Kelly, Sprafka, Edwards, & Griffith, 1994). Exposure to chlorpyrifos has also been associated with an increase in the occurrence of atopic conditions (Thrasher, Madison, & Broughton, 1993). These studies suggest that pesticide exposures could be important etiologic and morbidity-modifying factors in the occurrence of childhood asthma. Nonetheless, only two major studies of childhood exposures (not exclusively set in an agricultural environment) have shown associations between pesticides and asthma prevalence (Salam et al., 2004; Sunyer et al., 2006). In the school-based California study, exposure to herbicides or pesticides in the home during the first year of life was associated with a greater odds of children presenting with early persistent wheeze (OR=3.8, (1.7-8.40)) (Salam et al., 2004). In the Spanish study, diagnosed asthma and persistent wheezing were associated with the organochlorine and DDE at birth (for each 1 ng/ml increase, OR=1.18 [1.01-1.39] and OR=1.13 [0.98-1.30], respectively), but not with DDE at age 4 years (Sunyer et al., 2006).

New methodologies for exposure assessment: In 2006, the NIH established the Genes, Environment and Health Initiative (GEI) with the long range goal of providing a foundation of technology and knowledge to enable population scale studies on the interaction of genetic and environmental factors in human disease. At the outset of the GEI, it was determined that large

scale, broadly focused Gene-Environment interaction studies would require an improved capacity in exposure assessment. Specifically two aspects were identified, the first being the need for improved definition of exposure at the level of the individual and the second being a comprehensive view of the environment integrating an assessment of exposures and lifestyle factors.

The Exposure Biology Program is divided into four component areas: sensors for assessment of chemical exposures (SACE), diet and physical activity, psychosocial stress and addictive substances, and biological response indicators to each of these environmental agents. Each of these programs is working individually, with opportunities for cross-program collaboration, to develop a new set of tools which will address the most common limitations of the current technologies used for exposure assessment: indirect measurement, lack of temporal or spatial resolution, limitation to single endpoints and a high degree of obtrusiveness. Each of the programs is product oriented with a goal of delivering prototype devices and biomarker panels for field testing and validation at the end of the four year granting period. The Sensors for Analysis of Chemical Exposures (SACE) program within the Exposure Biology Program of GEI was developed to build a next generation of sensors for defining real-time exposure with the expectation that this will increase the power of environmental epidemiology and gene-environment interaction studies.

Through SACE, the NIEHS and NIH have funded eight projects to develop integrated sensor devices which include not only the capability to detect multiple analytes of interest in a highly time resolved manner, but also integrate on board data handling, GPS based localization and in a few cases activity pattern analysis as well. The projects are detecting a wide range of analytes including particulate matter (PM 10, 2.5 and 1), allergens (dust mite, cat, cockroach and more), pesticides, oxidants, molecular gases ($O_3$, COx, SOx, NOx), and volatile organic compounds (benzene, toluene, xylene, and high priority industrial pollutants). In summer 2010, CDC established an interagency agreement with NIEHS to use three types of these devices in each of the home visits in order to improve exposure assessment in the Green Housing Study and also validate their use. The details of the devices are described later in this section (section A1).

Outdoor air pollution: In laboratory studies, investigators often have the ability to carefully control exposures that might be related to health effects. Because this study is tethered to HUD's green renovations programs, randomization is not a feasible option for study site selection. Nonetheless, there are some factors such as outdoor air pollution which we can control by using GIS to match green buildings to comparison buildings. The greenest building located in a heavily polluted neighborhood (i.e., proximity to major roadways, airports, and bus depots) might have outdoor exposures that overwhelm any potential health benefit of the green attributes. Proximity to major roadways has been associated with high concentrations of particulate matter (PM) less than 10μm ($PM_{10}$) which is from coarse grinding activities and also with high concentrations of particles less than 2.5 μm ($PM_{2.5}$) which is associated with combustion sources (Liao et al., 2006). Moreover, proximity to major roadways is associated with emergency department (ED) visits (Tolbert, Klein, Peel, Sarnat, & Sarnat, 2007; Tolbert et al., 2000), asthma prevalence (van Vliet et al., 1997) and morbidity (e.g, lung function and bronchial hyperreactivity) (Brunekreef et al., 1997; Janssen et al., 2003), and allergy (Morgenstern et al., 2008). Specifically, the diesel exhaust particulates within the $PM_{2.5}$ fraction augment the

allergenicity of the particles (Diaz-Sanchez, 1997). This indicates the importance of GIS to match proximity to sources of PM for both site selection and statistical analysis.

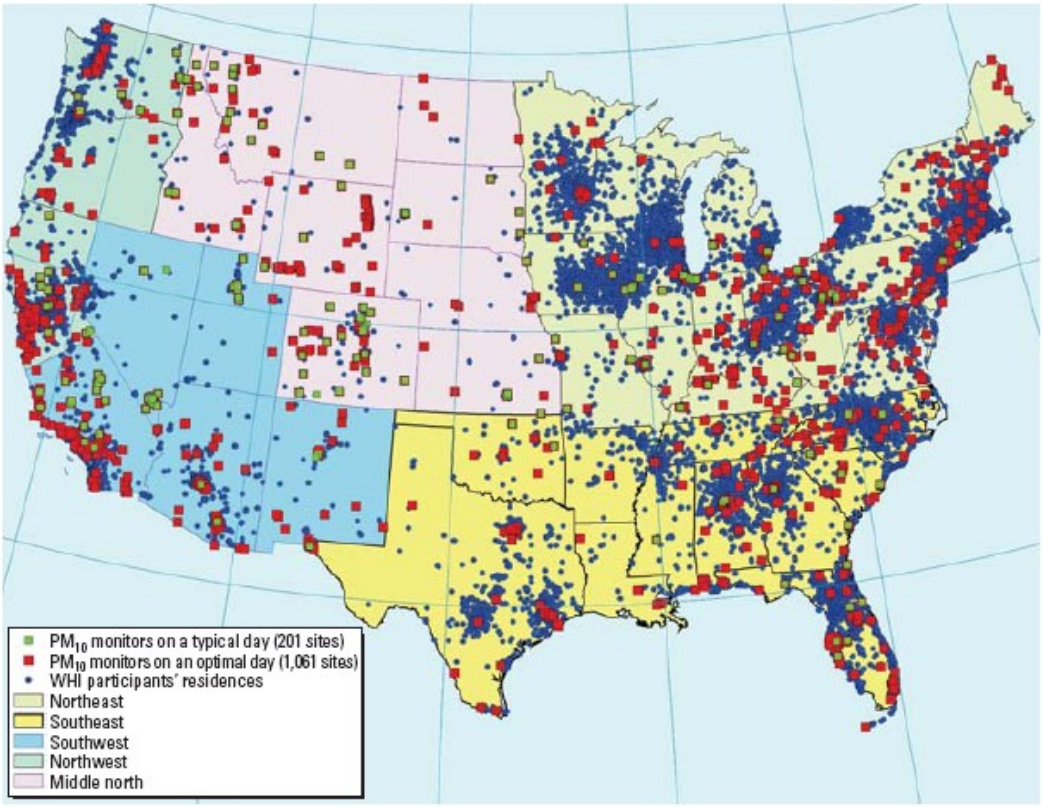



Figure 1. Spatial relationships between residential locations in a study by Liao et al. (2006) and EPA monitoring sites for $PM_{2.5}$ and $PM_{10}$.

The proposed study (*The Green Housing Study)* will address several of the research gaps that were mentioned above. The study participants are children with asthma (age 7-12 years). Comparison homes are those not currently receiving a green housing renovation (see inclusion criteria in Table 2 later in this section). The specific aims of this study are as follows:

1. To conduct an exposure assessment of chemical and biological contaminants, pesticides, volatile organic compounds (VOCs), fungi, indoor allergens (in terms of variety and concentration) in green vs. comparison housing.
   a. We will measure interior levels of pesticides in surface wipe samples; fungi and indoor allergens in dust samples; and VOCs in air samples.
   b. We will also compare levels of biomarkers of VOCs and pesticides (in terms of variety and concentration) from the participating residents of green and comparison housing.

2. To examine the relationship between living in green vs. comparison housing and asthma morbidity (e.g., symptoms, ED visits, use of medications, lost school/work days) of children with doctor-diagnosed asthma (ages 7-12 years). We will adjust for allergic sensitization and ETS.

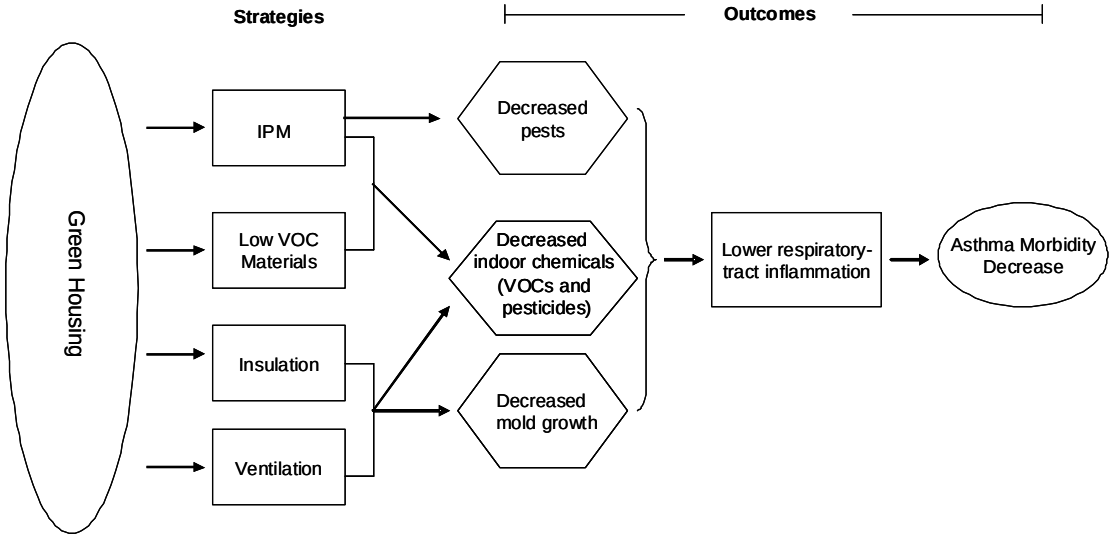



Figure 2. Hypothesized relationships among green housing rehabilitation strategies, environmental exposures, and asthma-related health outcomes.

The hypotheses of this study are as follows:

1. Green housing utilizes different strategies to reduce environmental contaminants. We hypothesize that these strategies will lead to 1) lower levels of environmental contaminants compared with those of comparison housing, and 2) lower levels of related biomarkers in the residents of green vs. comparison housing.

    a. Integrated pest management (IPM) is a method to reduce pests such as cockroaches and mice by eliminating entry points in the home and harborage areas.
        i. We hypothesize that IPM will result in lower cockroach and mouse allergen levels while at the same time lowering the concentrations and array of pesticides in the green vs. comparison homes.
        ii. We hypothesize that concentrations of pesticide metabolites in urine of children living in green housing will be lower than those living in comparison homes.

    b. The use of low VOC paints, carpeting, and other building materials contain lower concentrations of aldehydes, ketones, and alcohols.
        i. We hypothesize that the levels of VOCs will be lower at baseline in green-renovated vs. comparison homes.
        ii. We hypothesize that concentrations of VOCs in urine of children with asthma (ages 7-12 years) living in green housing will be lower than those living in comparison homes.

    c. Insulation can reduce sources of moisture, specifically condensation. We hypothesize

that green housing will have more and possibly better insulation (e.g., higher R-value) than comparison housing. We hypothesize that insulation (e.g., dual-paned windows, insulated cold water pipes, and rigid insulation above concrete floors and in exterior walls) will result in lower concentrations of dust mite (and therefore their allergens) and fungi.

d. Another aspect of green housing is improved ventilation which can reduce moisture and decrease indoor concentration of VOCs. For example, improved exterior wall insulation can reduce condensation and a properly-sized and maintained central heating, ventilating, and air-conditioning unit (HVAC) can help buildings keep dry and at the same time, exhaust environmental contaminants to the outside.

   i. We hypothesize that green housing will have a higher percentage of units with the recommended air exchange rates than comparison housing.
   ii. We hypothesize that green housing units will have lower VOCs than comparison homes.
   iii. We hypothesize that green housing units will have lower levels of fungi and dust mite allergen than comparison homes.

2. If irritants and allergens are lower in green vs. comparison housing, residents of green housing should experience decreased asthma morbidity. Specifically, we hypothesize that children with asthma (ages 7-12 years) in green housing will have lower asthma morbidity, adjusting for environmental tobacco smoke (ETS) exposure.

Privacy Impact Assessment

Below, we discuss three aspects of privacy impact assessment: (i) an overview of the data collection system, (ii) a delineation or listing of the items of information to be collected, and (iii) an indication of whether the system hosts a website.

Overview of the Data Collection System

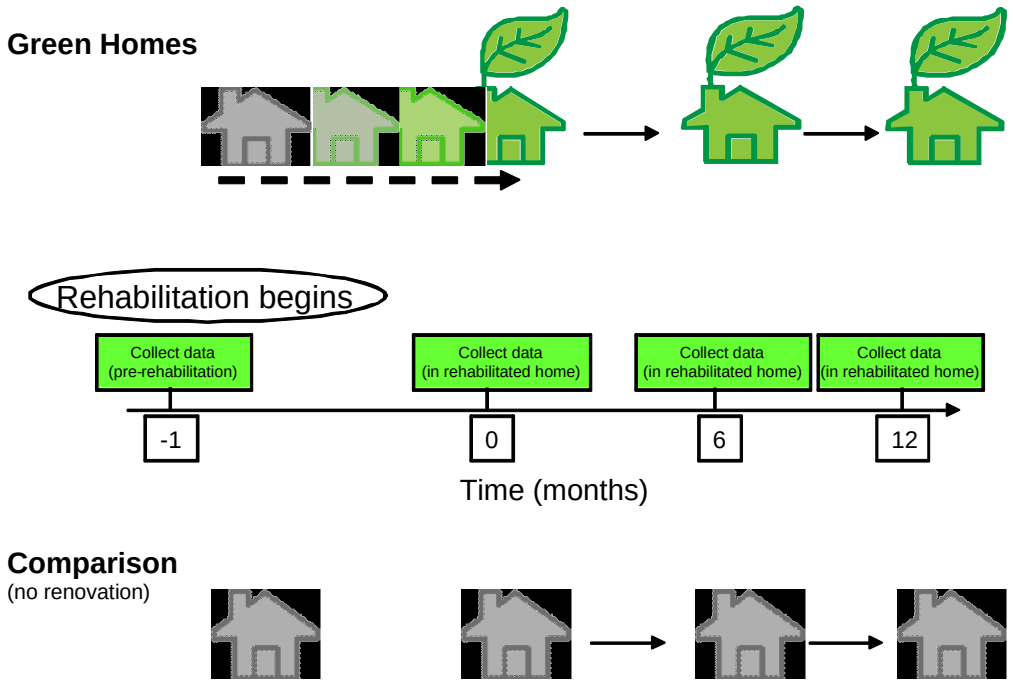
The United States Department of Housing and Urban Development (HUD) subsidizes both publicly- and privately-owned housing across the country, notably in urban areas. HUD requires that these subsidized properties be rehabilitated to maintain a certain level of habitability. CDC will leverage the opportunity to study rehabilitated properties in thirteen (13) study locations (large metropolitan areas that are located in different climactic regions of the United States). The selection criteria are described in Part B. From each of these geographically-stratified study sites, 32 green intervention homes and 32 comparison homes (total = 832) will be included. Within each study site (i.e., city), both the green-renovated and comparison homes will be from the same housing development or neighborhoods to ensure homogeneity with regard to housing type and other socioeconomic factors. Changes in environmental measurements (pesticides, VOCs, particulate matter (i.e., PM 2.5 and 1.0), indoor allergens, and fungi) over the 1-year follow-up in both types of housing (green intervention and comparison) will be compared, thus each home's follow-up measurements will be compared with its own baseline exposure level. This two-group pre-post within-group and between-group comparison will increase ability to detect differences in exposure levels and asthma outcomes that might result from the green renovations in our study. At this time, these sites have not been determined by HUD and CDC.

**Appendix C (The IRB-approved Protocol)**

When the study sites are selected, the data collection partners will include: 1) CDC; 2) HUD, and 3) contracted research institutions (to be determined).

In Figure 3, we describe a scenario of how measurements collected in green-renovated homes would be compared to: 1) those of the baseline, 2) those of homes without any renovation at all. Residents will participate for 1 month prior to rehabilitation, the time required for rehabilitation of their home (usually just a few days), and 12 months after completion of the rehabilitation. The duration of the participation for the residents of comparison homes is the same except no renovation will occur. More details of the study design are provided in Part B of this information request.

Figure 3. Diagram of renovation schedule (green intervention vs. comparison)




Eligible participants will be limited to children with doctor-diagnosed asthma (ages 7-12 years). Health information for eligible children will be reported by the mother/primary caregiver living in HUD-subsidized housing that either received a green renovation (i.e., green intervention) or living in HUD-subsidized housing that received no renovation at all (i.e., comparison). Details of the eligibility criteria are listed in Table 2.

Table 2. The Green Housing Study's inclusion and exclusion criteria

| Inclusion Criteria | Exclusion Criteria |
|---|---|
| 1. Children (age 7-12 years with asthma)<br>- Mother/ primary caregiver reports that child has ever been diagnosed with asthma by a physician and child has experienced asthma-related symptoms (wheezing, slow play or night awakening) during the past 6 months.<br>2. Mothers/primary caregivers of the children listed above.<br>- No clinical markers will be collected, but we will ask questions regarding their home environment that might be related to child's health outcomes of interest.<br>3. Green homes will be renovated using low VOC materials and integrated pest management (IPM) principles. | 1. Health condition (e.g., Cystic Fibrosis) that would make it difficult to participate in lung function tests.<br>2. Does not live in housing complex on average 7 days per week.<br>3. Plans to move before the 1-year follow-up of study is completed.<br>4. Mother/ primary caregiver does not speak English, Spanish, or Chinese |

Residents who express interest in the study can contact the site projector coordinator by telephone or e-mail. Subsequently, subcontracted staff (trained by the CDC study investigators) will schedule a home visit with the residents. During this home visit each resident's eligibility will be assessed (i.e., the Screening Form will be filled out by the aforementioned staff based on responses from the mother/ primary caregiver). If a child is eligible, then the study will be explained to the mother/ primary caregiver, and if they are willing to participate, individual participant consent will be obtained from the mother/ primary caregiver. Child assent will be obtained from all children 7-12. The children ages 7-12 will be assenting to provide blood and urine samples for the study; they will not be asked to respond to survey questions—their mothers/ primary caregivers will be providing that information. Consent and Assent forms are in Appendices F and G. After consent and assent as appropriate is obtained, the technicians will collect all of the study baseline information during the initial visit. Participants will receive monetary compensation for participation as outlined in section A.9 (Explanation of Any Payment or Gift to Respondents).

The methods of data collection will include written survey data collected through personal telephone, and text messaging interviews of enrolled mothers/ primary caregivers (Table 8). Trained staff will visit each enrolled child's home four times (including the initial visit to obtain consent and baseline measurements) during a 1-year period to administer a battery of questionnaires. Each of the surveys will be administered in-person to the enrollee's mother/ primary caregiver in the study by bilingual (English and Spanish or English and Chinese) interviewers. In addition, brief text messages to inquire about respiratory infections will be sent at the end of months 1, 2, 4, 5, 7, 8, 10, and 11. The enrollee's mother/ primary caregiver will also be contacted by phone at two time points during the same 1-year period just to update

contact information and inquire about respiratory morbidity. Enrolled children (ages 7-12 years) will not be interviewed; however, their mothers/ primary caregivers will provide information about their children's exposures and health outcomes.

Table 3. Surveys administered during a 1-year period

| Type of Survey/ Form | | Responses of the Mother/ Primary caregiver (regarding the participating child with asthma age 7-12 years) |
|---|---|---|
| Screening | | 10 minutes |
| Baseline Questionnaire | Home Characteristics | 15 minutes |
| | Demographics | 15 minutes |
| | Children with asthma 7-12 years | 15 minutes |
| Monthly Texts about child's respiratory symptoms (occurs during months when phone or home visit not conducted) | | 1 minute (eight time points) = 8 minutes |
| 3 and 9-month Phone contact | | 5 minutes (two time points) = 10 minutes |
| 6 and 12-month Follow-up Questionnaire | Environment | 10 minutes (two time points) = 20 minutes |
| | Mother/ primary caregiver | 10 minutes (two time points) = 20 minutes |
| | Children with asthma 7-12 years | 10 minutes (two time points) = 20 minutes |
| Time/Activity | Mother/ primary caregiver | 5 minutes (four time points) = 20 minutes |
| | Children with asthma 7-12 years | 5 minutes (four time points) = 20 minutes |
| | | |
| Total Number of surveys | | 27 |
| Estimated response time during a 1-yr period | | 163 minutes |

All paper copies of consent forms and questionnaires will be scanned into electronic files. The paper copies of the data will be maintained at each study site's contracted research institution (to be determined) for a period of 5 years beyond the last peer-reviewed publication of the results. At that time, paper copies will be shredded and then recycled. The electronic files will be shared with CDC, and CDC will keep the electronic files in accordance with approved record control schedules.

Health and Environmental Assessments:

- For Intervention Homes: Summaries of the clinical and environmental measurements are shown in Tables 4 and 5. The baseline measurement will occur up to one (1) month prior to commencement of rehabilitation activities. Baseline part 2 will be collected in the home one (1) week after completion of rehabilitation activities. Total time of study participation is approximately 1 year, although the exact time will vary depending upon the rehabilitation scenario. Residents will participate for 1 month prior to rehabilitation, the time required for rehabilitation of their home, and 12 months after completion of the rehabilitation. Estimated time for rehabilitation activities (e.g., new paint, carpeting, Energy Star appliances, IPM) should be only a few days.

- For Comparison Homes: The baseline measurement will occur within one (1) week either before or after the baseline measurements were taken from the matched intervention home. Baseline part 2 will be collected in the home within one (1) week either before or after the baseline part 2 measurements were taken from the matched intervention home. Total time of study participation is approximately 1 year, although the exact time will vary depending upon the rehabilitation scenario. Residents will participate for the same amount of time as the matched group of intervention homes.

Table 4. Summary of clinical measurements

| Factor | Child with asthma (Age 7-12) |
|---|---|
| Blood | |
| Baseline | ✓ |
| Urine | |
| Baseline | ✓ |
| Baseline (part 2 occurs after renovation is completed) | ✓ |
| 6-mo. follow-up | ✓ |
| 12-mo. follow-up | ✓ |
| Pulmonary Function Test | |
| Baseline | ✓ |
| Baseline (part 2 occurs after renovation is completed) | ✓ |
| 6-mo. follow-up | ✓ |
| 12-mo. follow-up | ✓ |
| Exhaled Nitric Oxide | |
| Baseline | ✓ |
| Baseline (part 2 occurs after renovation is completed) | ✓ |
| 6-mo. follow-up | ✓ |
| 12-mo. follow-up | ✓ |
| Respiratory Symptoms Questionnaire | |
| Baseline | ✓ |
| Baseline (part 2 occurs after renovation is completed) | ✓ |
| 6-mo. follow-up | ✓ |
| 12-mo. follow-up | ✓ |

*Blood will be used for assessment of allergy status (IgE)
**Urine will be used for assessment of cotinine (marker of ETS exposure), pesticides, and VOC metabolites

Table 5. Summary of environmental measurements in homes*

| Type of assessment | Baseline | Baseline part 2 (after renovation is completed) | 6-Month follow-up | 12-Month follow-up |
|---|---|---|---|---|
| Allergens | ✓ | ✓ | ✓ | ✓ |
| Fungi | ✓ | ✓ | ✓ | ✓ |
| Pesticides | ✓ | ✓ | ✓ | ✓ |
| VOCs | ✓ | ✓ | ✓ | ✓ |
| Particulate Matter ($PM_{2.5}$) | ✓ | ✓ | ✓ | ✓ |
| Temperature | ✓ | ✓ | ✓ | ✓ |
| Relative Humidity | ✓ | ✓ | ✓ | ✓ |
| Air Exchange Rate | ✓ | ✓ | ✓ | ✓ |

*The mother/ primary caregiver's home is the same as that of the child. Dust sampling will occur in kitchens and the children's beds as well as those of the mother/ primary caregiver. The mother/ primary caregiver bed is sampled because it serves as a proxy of exposure to several of the indoor allergens. This proxy can help with characterization of the indoor environment especially in cases where limited dust is available from the child's bed. Except for the pesticide measurements in the kitchen, all other measurements will be limited to the child's bedroom.

Assessments for children: Upon enrollment, the technicians (with training provided by CDC) will collect all of the study baseline information from the primary caregiver during the initial visit. This includes: a home characteristics questionnaire, an environmental exposure assessment, and health questionnaire. For those children (age 7-12) who meet asthma inclusion criteria, we will also collect urine samples, a blood sample, nasal and throat swabs for assessment of acute respiratory illness (ARI), exhaled nitric oxide (eNO), and conduct pulmonary function testing by spirometry. Details regarding these assessments are provided below.

Questionnaires: Information will be collected on frequency and duration of asthma-related symptoms, healthcare utilization, school and work absences, and medication use. The home characteristics questionnaires administered to the enrollee's mother/ primary caregiver will inquire about the type of building, heating and cooling of the home, furnishings, cleaning regimens, the presence of pets and pests, environmental smoke, and reports of dampness. Provenance of the questions is described in Part B.

Temperature and Relative Humidity Measurements: Temperature and relative humidity measurements for each home will be obtained during each home visit. A HOBO® continuous data logger (Onset Computer Corporation, Bourne, MA) will be placed on the floor in each home's living room for one week, and continuous measurements (every 5 minutes) of temperature and relative humidity will be recorded.

Dust sampling: Sampling for allergens and fungi will be carried out by technicians using a standardized protocol. All field staff will be trained by CDC in the proper methods for sample collection and handling. Dust samples will be collected separately from kitchens and beds by using a canister vacuum cleaner. One dust sample will be collected from the kitchen, focusing on the baseboard area and perimeter of the oven and refrigerator, for a duration of 3 minutes.

Another dust sample will be collected from the index child's bed. Finally, a third dust sample will be collected from the bed of the mother/ primary caregiver. The mattress and pillows associated with the upper half of the bed will be vacuumed for 3 minutes. After sampling, each filter will be sealed in a sterile plastic tube and stored at -20ºC until analysis for indoor allergens and fungi.

Indoor allergen analysis: Frozen dust samples will be transported to the laboratory at CDC. Samples will be analyzed dust mite (Der f 1 and Der p 1), cockroach, (Bla g 2), cat (Fel d 1), dog (Can f 1), rat (Rat n 1), and mouse allergens (Mus m 1) using commercially available multiplex immunoassays (Indoor Biotechnologies, Charlottesville, VA).

Fungi analysis: Dust samples from the beds will also be analyzed for a total biomass marker of fungi, ergosterol, by gas chromatography/mass spectrometry (GC/MS) (Park et al., 2008).

Volatile organic chemicals (VOCs): Continuous air monitoring will be conducted using passive diffusion dosimeters for VOCs (one for solvents and one for aldehydes). The passive dosimeters will be placed in each participating home for 5 days. Total VOCs will be quantified using GC/MS. Aldehydes will be desorbed from passive 2,4-dinitrophenylhydrazine (DNPH) treated media, and the derivatized aldehydes are to be analyzed by high-performance liquid chromatography (HPLC) (Adgate et al., 2004).

Pesticides: Dust samples will be collected by wiping a measured 12-inch square section of the floor along the baseboard in the kitchens. Samples will be gathered on gauze squares wetted with isopropanol and will be analyzed using GC/MS and HPLC/MS (Table 6). Common pyrethroid (*cis*- and *trans*-permethrin, cyfluthrin), organophosphate, and carbamate pesticides will be analyzed in addition to a synergist that is used uniquely in pyrethroid pesticides (piperonyl butoxide).

Table 6. A list of pesticides that EPA can measure in environmental samples.

| Organochlorines | Pyrethroids/Pyrethrins |
|---|---|
| α- and γ- Chlordane | Allerthrin |
| Heptachlor | Bifenthrin |
| P,p=DDT | Cyfluthrin I, II/III, IV |
| P,p=DDE | Cypermethrin I, II/III, IV |
| Organophosphates | Deltamethrin |
| Chlorpyrifos | Esfenvalerate |
| Diazinon | Fenpropathrin |
| Malathion | Imiprothrin |
| Phenyl-Pyrazole | Λ-cyhalothrin |
| Fipronil | *Cis*- and *trans*-Permethrin |
| Other | Pyrethrin I, II |
| Piperonyl Butoxide | Prallethrin |
| | Resmethrin |
| | Sumithrin |
| | Tetramethrin I, II |

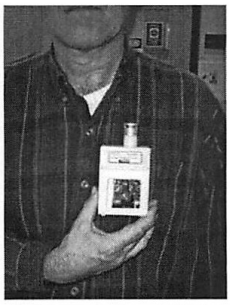
Air Exchange Rates (AER): Air exchange rates can be quantified using non-toxic tracer gases such as $SF_6$ and perfluorinated methylcyclohexane (PMCH). The method to be employed in this study will use the perfluorocarbon, PMCH. In brief, the method is accomplished by placing a sponge with a nontoxic tracer gas inside the home and allowing the gas to reach steady state (Dietz et al., 1982). With passive air sampling for a period of 12 hours up to one week, the PMCH is collected and then analyzed by gas chromatography and electron capture detector (GC/ECD). The range of quantification is 0.10 to 2.5 air changes per hour (ACH), and the upper limit of detection is about 3.0 ACH.

Particulate ($PM_{2.5}$) Monitoring: Monitoring for particulate matter ≤ 2.5 μm ($PM_{2.5}$) will be conducted in the child's bedroom(at a height of 1.5 meter) using integrated sampling for a one week period during each home visit in order to enable for adjustment of seasonal variation (Breysse et al., 2005). Integrated samples will be collected using constant airflow portable sampling pumps designed for quiet indoor operation. Samples for $PM_{2.5}$ will be collected on 37 mm, 1.0 μm pore-size PTFE membrane filters using single-stage Personal Modular Impactors (SKC, Inc.). The pump flow-rate will be calibrated at a flow rate equal to 3 L/min in the laboratory prior to the start of sampling and checked at the end of sampling with a BIOS DryCal DC-2 flow meter.

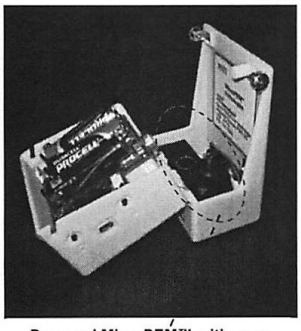
Outdoor air sampling: To obtain an estimate of outdoor PM and VOC exposure for each of the housing developments, we will conduct 1-week air sampling on rooftops under protected cover during winter, spring, summer and fall. These measurements will be repeated throughout the entire study period for a given city. These repeated measures should yield a better estimate of the average outdoor PM and VOC exposure and reduce the influence of local events that might give rise to extreme values.

Opportunity for real-time exposure assessment of VOCs and PM: CDC has an interagency agreement NIEHS to provide field-deployable units that measure particulate matter with an aerodynamic cutpoint of 2.5 μm ($PM_{2.5}$), 1.0 μm ($PM_{1.0}$), and VOCs to be used for field validation in a study of the potential environmental and health benefits associated green eco-friendly construction and maintenance practice in the Green Housing Study. These devices were developed as part of the NIH's Gene- Environment Initiative (GEI), specifically the Sensors for Assessing Chemical Exposures (SACE program). NIH will provide up to five (5) field-deployable units from each of the selected SACE investigators that have developed sensors which are both 1) field-deployable and 2) capable of measuring analytes relevant to the Green Housing Study. These devices will collect measurement side-by-side with the traditional air sampling devices during each of the home visits. The advantage of these devices is that they can measure peaks of exposure that might not be captured with traditional integrated air sampling equipment. The peaks might be more closely related to the biomarkers that will be collected (e.g., VOC metabolites in urine and exhaled nitric oxide). Figures 4, 5, and 6 below describe the three devices that will be used in the Green Housing Study.

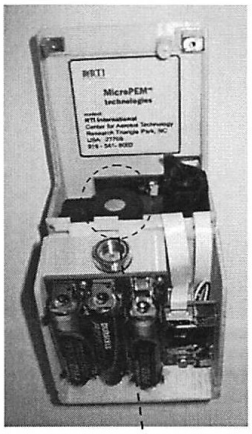
Figure 4. The single-channel real-time $PM_{2.5}$ monitor that will be used in the Green Housing Study.



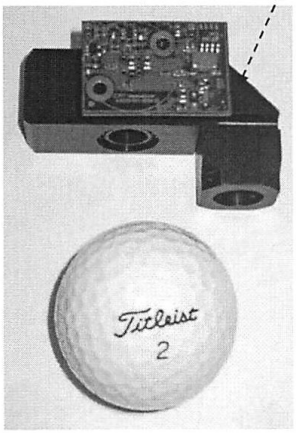
RTI personal MicroPEM™ (scalable version) showing relative size; inlet location



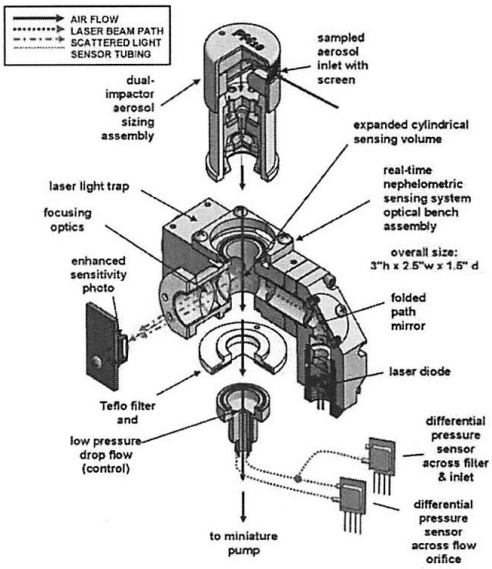
Personal MicroPEM™ with case opened showing nephelometric optical bench location (no filter)



Personal MicroPEM™ showing AA batteries, coin-cell memory battery; and Teflo filter/holder installed in outlet




Personal MicroPEM™ optical bench shown with golf ball to illustrate overall size of prototype




Personal MicroPEM™ optical bench showing: a) inlet/impactor assembly, b) filter/holder assembly, and c) flow and laser beam paths; note extremely large 10 mm cross-section sensing volume

**Appendix C (The IRB-approved Protocol)**

Figure 5. The dual-channel real-time $PM_{1.0}$ and $PM_{2.5}$ monitor that will be used in the Green Housing Study.

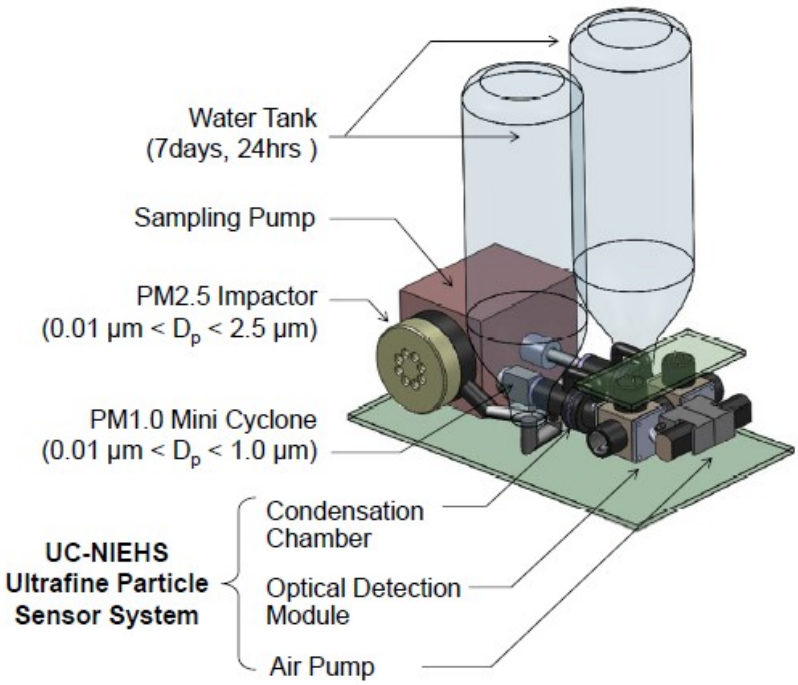



Figure 6. The real-time VOC monitor that will be used in the Green Housing Study.

Urine collection: Urine will be collected for two main purposes: 1) to assess recent ETS exposure via cotinine measurement); and 2) to assess biomarkers of pesticides and VOCs (Tables 7 and 8). Urine analysis will be conducted by CDC's National Center for Environmental Health, Division of Lab Sciences using standard methods (Baker et al., 2000, Matt et al., 1999, Ding et al., 2009).

Table 7. Urinary metabolites of VOCs measured by the CDC's Division of Laboratory Sciences

| | Compound | Parent Chemical |
|---|---|---|
| DHBMA | N-Acetyl-S- (3,4-Dihidroxybutyl)-L-Cysteine | 1,3 Butadiene |
| MHBMA | N-Acetyl-S- (1-Hydroxymethyl)-2-propenyl-L-Cysteine | 1,3 Butadiene |
| CBMA | N-Acetyl-S- (2-Carboxyethyl)-L-Cysteine | Acrolein |
| HPMA | N-Acetyl-S- (3-Hydroxypropyl)-L-Cysteine | Acrolein |
| HEMA | N-Acetyl-S- (2-Hydroxyethyl)-L-cysteine | Acrylonitrile, Bromoethanol, chloroacetaldehyde, ethylene, chloroethylene, 1,2-dichloroethane, ethylene oxide, 1,2-dibromoethane, vinyl chloride |
| PMA | N-Acetyl-S-(phenyl)-L-cysteine | Benzene |
| BMA | N-Acetyl-S- (benzyl)-L-Cysteine | Toluene |

Table 8. Urinary metabolites of pesticides measured by the CDC's Division of Laboratory Sciences

| Compound | Parent Chemical |
|---|---|
| *cis*-2,2-(Dichloro)-2-dimethylvinyl cyclopropane carboxylic acid) (*cis*-DCCA) | Permethrin, cypermethrin, cyfluthrin |
| 4-Fluoro-3-phenoxybenzoic acid (4F3PBA) | Cyfluthrin |
| Carbofuranphenol (2,3-dihydro-2,2-dimethy-7-hydroxybenzofuran) (CFP) | Carbofuran, benfuracarb, carbosulfan |
| 2-Isopropoxyphenol (IPP) | Propoxur |
| 2-Isopropyl-4-methyl-6-hydroxypyrimidinol (IMPY) | Diazinon |
| *para*-Nitrophenol (PNP) | Parathion, methyl parathion, nitrobenzene |
| 3,5,6-Trichloro-2-pyridinol (TCPy) | Chlorpyrifos |

Blood collection: Blood will be collected to assess allergic sensitization (described below). A 10-ml sample (i.e., 2 teaspoons) of venous blood will be collected into 2 tubes (tubes with coagulant for serum collection) by a trained phlebotomist. The tubes will be centrifuged within 2 hours of collection, serum will be aliquoted into sterile microcentrifuge tubes, and then frozen at -80$^{o}$C until they can be assayed for total and allergen-specifc IgE titer.

Allergy testing: Allergen testing will be performed once at baseline following enrollment. We will use immunoCAP method to assess total and allergen-specific (dust mite, cockroach, cat, mouse, tree mix, grass mix, and weed mix) IgE antibodies in serum. Unfortunately, mold extracts used for measuring IgE are very poor (due to batch-to-batch variability), thus we will not be able to assess sensitization to mold.

Pulmonary function testing: Pulmonary function provides an objective outcome for determining improvements in respiratory health status following the intervention to decrease environmental asthma triggers in the home and improve asthma management. Spirometry (pulmonary function testing or PFTs) will be performed in children with a diagnosis of asthma who are 7-12 years of age. Study participants will be weighed and their heights will be measured using a calibrated scale prior to the start of each testing session. Standard spirometric measures, forced vital capacity (FVC), forced expiratory volume in 1 second ($FEV_1$), the ratio of $FEV_1$/FVC, forced expiratory flow between 25-75% of vital capacity ($FEF_{25-75\%}$), and peak expiratory flow (PEF), will be recorded for each patient (Hankinson et al., 1999). All children in this age range may not be able to successfully complete the forced expiratory maneuver required for this test, but

attempts to test all children in this age range will be made. All PFT studies will be performed at each home visit to assess possible seasonal variation.

We will not conduct lung function tests on asthmatic children who are in distress; we will reschedule the visit. It is our experience that a phone call to the home approximately 1 hour before the scheduled visit serves not only as a reminder that our research assistants will be visiting the home, but also as an opportunity to inquire if the child will be at home and is ready for the tests (such as lung function, blood draw, etc). If during this phone call, the mother/ primary caregiver indicates that the child is in respiratory distress, then we will advise her to hang up and attend to her child and if necessary seek medical attention.

The technician who administers the lung function test in the home is not qualified to determine if the child's lung function is impaired; accurate interpretation of test results requires review by a trained pediatric pulmonologist. We expect that it would take at least 2-3 months for the pulmonologist (site-specific) to review the lung function curves (typically done in batches)—by that time the lung function could have changed for that child. Lung function tests done in isolation (and at any given timepoint) without consideration of other clinical parameters are difficult to interpret. Therefore, we will mail the results of each of the lung function tests (as they become available) to the mother/ primary caregiver after review by the pulmonologist. The mother/ primary caregiver can then share this information (i.e., repeated lung function tests) with the child's healthcare provider who can better interpret the lung function test results within the context of other relevant parameters (such as recent medication use) that would affect the child's overall asthma management. These results will be provided to participating asthmatic children of both the green and comparison homes to avoid potential bias.
Documentation of the participating asthmatic child's primary care provider will occur at the baseline home visit and participants who do not identify a primary care provider will be referred to one in their local area. A participant who contacts study staff with acute health concerns will be referred to his/her primary care provider or the Emergency Department.

Exhaled Nitric Oxide (eNO): eNO is a known marker of pulmonary inflammation and will provide a non-invasive means of assessing pulmonary inflammation in a large cohort that includes children (Buchvald et al., 2005; Cardinale et al., 2005; Pijnenburg, Hofhuis, Hop, & De Jongste, 2005). Measurement of exhaled nitric oxide will be obtained prior to lung function, and will be obtained according to the American Thoracic Society Guidelines (ATS, 2005). Nitric oxide concentrations will be measured using a chemiluminescent analyzer (NIOX TM System, Aerocrine, Sweden). This equipment is FDA-approved for clinical use in asthma management. Participants will be required to produce at least two reproducible exhalations.

Nasal and throat swabs: Children with asthma are commonly exposed to multiple indoor allergens and environmental tobacco smoke, multi-factorial exposures that may contribute to the increased asthma-related complications in this population. However, previous studies of environmental interventions for patients with asthma have not used objective measurements (i.e., PCR of nasal swabs) accounted for the role of acute respiratory illness (ARI) as triggers for asthma exacerbation (Morgan et al., 2004). Viral respiratory tract infections have been reported as important triggers for exacerbations of asthma in adults and children (Clark, 1979, Miller et al., 2008). Recent studies based on PCR assays support an important role of viral respiratory

tract infections in acute asthma exacerbations (Khetsuriani et al., 2007). By accounting for the role of respiratory virus infections as triggers for asthma exacerbation, we may be able to find stronger associations when aiming to estimate the impact of environmental interventions on improvement of symptoms of asthma and decrease use of health care services. This is because respiratory virus infections may be associated (or interact) with study's outcome and exposure measures, underestimating the effect of the intervention.

Mothers/primary caregivers of the participating children with asthma will be trained to collect one nasal swab and one throat swab after 24-36 hours from onset of at least three of the following: fever, stuffy/runny nose, cough, sore throat, body aches, or tiredness, for more than 24 hours. It is estimated that children in this age group may have on average 4-5 episodes of ARI per year (Monto 2002). The specimens and an illness checklist will be collected on each occasion of a suspected ARI by using methods previously described by researchers (Esposito et al., 2010). The specimens can be stored in the participant's refrigerator for up to one week before being picked up by the study coordinator. The study coordinator will be asked to collect the specimens within 1-2 days of being notified of the parent-collected specimens. At the time of swab pick-up, the trained research assistants will also collect a throat swab and another nasal swab from the child in order to validate the sample collected by the parent. The swabs will be combined and transported in either veal infusion broth (VIB) or Hank's transport media on ice to the laboratory processing (within 24 hours). The specimens will then be stored at -70 C at local laboratory facilities before being sent to CDC. Specimens would be tested by RT-PCR for RSV, rhinovirus, influenza viruses, parainfluenza viruses, adenoviruses and human metapneumovirus at CDC's Viral Respiratory Laboratory.

Assessment for mothers/ primary caregivers of children: The only measurement obtained will be questionnaire data regarding the impact of demographic characteristics and behaviors on the respiratory health of the participating child. Such behaviors include but are not limited to: smoking, cooking, and working in environments that could conceivably result in passive transport of chemicals and allergens.

Items of Information to be Collected

Data to be collected about the study participants will include: contact information, demographics, housing characteristics, environmental exposures, health outcomes, and healthcare utilization as listed in questionnaires (Appendices D1-13). We describe the Information in Identifiable Form (IFF) in Table 9.

Table 9. Information in Identifiable Form (IIF) collected during this study.

| IIF category | Collected by grantee but not sent to CDC | Collected by grantee and sent to Green Housing Study staff at CDC |
|---|---|---|
| name | X | |
| date of birth | | X |
| phone numbers | X | |
| medical information and notes | | X |
| biological specimens | | X |
| e-mail address | X | |
| employment status | | X |
| home address | | X |

CDC requires the home address in order to geocode the home and adjust for influence of outdoor air pollution. (See section A10 for details).

Identification of Website(s) and Website Content Directed at Children Under 13 Years of Age
There is no website associated with this study. Therefore, there is no website content directed at children under 13 years of age.

A.2. Purpose and Use of Information Collection

The specific aims of this study are to: 1) conduct an exposure assessment of chemical and biological contaminants, pesticides, volatile organic compounds (VOCs), fungi, and indoor allergens in green vs. comparison housing; and 2) examine the relationship between living in green vs. comparison housing and asthma morbidity. Publications of the study results have the potential to be cited frequently by other researchers, and both CDC and HUD can use data from the Green Housing study to guide their Healthy Homes grantee's activities via annual conferences and funding opportunities. In Table 10 below, we have justified the data collection in terms of positive needs and the negative consequences of not having the information, and we have emphasized the practical utility of the expected results to federal, state and local governments

Table 10. Justification and practical utility of the data collection.

| Type of data collected | Positive needs for having the information | Negative consequence of not having the information | Practical utility to the government of the expected results |
|---|---|---|---|
| Environmental exposures | This data will provide a direct measurement of environmental exposures in the homes of this sample of residents. | Merely having health data will not allow us to know if any meaningful differences in health status were truly associated with differences in chemical/biological exposures that were related to green housing factors. One could assume that because health symptoms are improved, that the exposures would have been lower, but this would only be an assumption. | This study will help CDC and HUD programs to advise their healthy homes, asthma, and child health grantee on which green criteria (if any) are positively associated with lower exposures. Subsequently, this will help grantee inform residents about which green housing practices and materials (if any) to implement in their homes not only for energy efficiency, but for lower exposures in their home, a place where people spend a significant proportion of their time. |
| Health status | This data will provide a direct measurement of health effects in this sample of residents. | Merely having exposure data will not allow us to know if any meaningful improvements in health status will occur with green housing factors. One could assume that because exposures are lower, that the health would be better, but this would only be an assumption. | This study will help CDC and HUD programs to advise their healthy homes and asthma grantee on which green criteria (if any) are positively associated with health outcomes (e.g., asthma outcomes). Subsequently, this will help grantee inform residents in their communities on which green housing practices and materials (if any) to implement in their low-income urban multi-family homes not only for energy efficiency, but for improved health e.g., asthma outcomes). |
| Healthcare utilization | This data will provide a direct measurement of healthcare utilization by this sample of residents which enables us to more fully capture the | If we did not collect data on healthcare utilization, then we would not be able to fully capture the burden of adverse health outcomes. | This will help CDC identify possible alternatives to pharmaceuticals to decrease healthcare costs among low-income urban |

| | | | |
|---|---|---|---|
| | burden of adverse health asthma outcomes. | | populations. It will inform Center for Medicare and Medicaid Services policies related to re-imbursement for preventative measures. |
| Home Address | We need to geocode the address so that we can use it to adjust for influence of outdoor air pollution. EPA currently has outdoor air pollution monitors in cities across the US. By knowing the exact location of our study participants' homes, we can use EPA's regional measurements in our statistical models of exposure and health outcomes. | There is the possibility that even the greenest of homes could be located in a highly-polluted area which could overwhelm any potential health benefits of green housing factors.<br><br>If we do not adjust for outdoor air pollution, then we will not be able to tease out any effects of indoor green housing factors on respiratory symptoms of the study participants. | Adjusting for outdoor air pollution will allow CDC and HUD to attribute improved respiratory health effects to green housing factors if they indeed exist. Subsequently, CDC and HUD can make informed recommendations about green building materials and practices that are connected to improved health outcomes. These recommendations could vary by city depending upon levels of outdoor air pollution. |
| Date of birth | We need to know the age of participants because age can influence health outcomes such as pulmonary function. | If we were to ask contracted entities to strip the date of birth and give CDC only age, we believe that some data might come to us in a truncated/rounded form and this would make our statistical models inaccurate. To preclude differences by reporting site, CDC would have better control of modeling this very important variable. | Accurate modeling of data is paramount to federal agencies defending and promoting their policies and recommendations. |

HUD has committed funds for the Green Housing Study to CDC via Interagency agreement (IAA) # I-PHI-01062. This IAA commitment for the next several years also leverages personnel and laboratory resources from CDC.

The proposed study will be conducted in low-income housing primarily in urban environments which is likely to have implications for the generalizability of our findings to suburban and rural residences. Also, it may not be appropriate to generalize our findings to children in families with higher socioeconomic status. However, this study will have the potential to improve the health outcomes of some of the most sensitive populations (low-income children with asthma).

**Appendix C (The IRB-approved Protocol)**

Privacy Impact Assessment Information

The IIF collected during the course of the Green Housing Study is listed below in Table 11. While most of the IIF collected is for enrollment and follow-up activities, some data can be sensitive and will be described in detail below.

Table 11. Information in Identifiable Form (IIF) and intended uses

| IFF category | Collected by grantee but not sent to CDC | Collected by grantee and sent to Green Housing Study staff at CDC | Collected by grantee and sent to CDC Green Housing Study staff, then sent to EPA pilot study add-on to the Green Housing Study staff | Purpose |
|---|---|---|---|---|
| name | X | | | Names are required for written informed consent. In addition, names aid both the study participant and the data collector during in-person and telephone questioning. |
| date of birth | | X | | To determine eligibility and to also adjust for age in statistical analysis. |
| phone numbers | X | | | To administer phone questionnaires. |
| medical information and notes | | X | X | To assess health outcomes for statistical analysis. |
| biological specimens | | X | X | To assess health-related biomarkers for statistical analysis. |
| e-mail address | X | | | To serve as a secondary means of contacting study participants to administer questionnaires and schedule home visits for sampling. |
| employment status | | X | X | To adjust for possible chemical exposures that could occur in the occupational environment. |
| home address | X | | | To enable grantee to visit homes. |
| Global Positioning System (GPS) Coordinates | | X | X | To enable adjustment for factors external to the home which could influence both exposures and health outcomes (e.g., outdoor air pollution). |

Data security and privacy will comply with all applicable institutional and legal requirements. Files (paper and electronic) will be physically protected at all times. Electronic files will be stored on secured servers with password protection. All paper copies of consent forms and questionnaires are scanned into electronic files. The paper copies of the data are maintained at each study site's research institution for a period of 5 years beyond the last peer-reviewed publication of the results. At that time, paper copies will be shredded and then recycled. Dates of birth and home addresses are primary direct identifiers and the grantee's removal of other direct identifiers (such as name, phone numbers, e-mail addresses) will minimize identification but not completely eliminate it. A unique Study ID will be assigned by the grantee as a key identifier for all study forms.

The electronic files are shared with CDC, and CDC will keep the electronic files in accordance with approved record control schedules. The electronic files contain date of birth, medical information, employment status, and home address, and identified by study ID number. The environmental and biological samples and measurements, as well as GPS/accelerometer data, will only be identified by study ID. While we acknowledge that home address is a unique identifier and the data collectors have the link to names and address, CDC Green Housing Study investigators have taken steps to reduce the amount of individually-identifiable data maintained at CDC.

Data file transfers to and from Green Housing Study investigators at CDC will use federal government approved (FIPS 140-2) encryption. Data will be stored on highly-secured CDC servers in Atlanta, GA. The servers are housed in a secure computer room complete with climate control, emergency power, and an uninterruptible power supply (UPS). Daily back-ups and integrated security are implemented through the CDC computer services infrastructure. All servers and PCs that are part of the CDC infrastructure are protected by both host-based firewalls and ant-virus software in order to protect against malicious software and other threats to data confidentiality, integrity and availability. CDC also employs intrusion detection systems (IDS), vulnerability scanners, and other tools to continuously monitor its IT system data, as well as incident response plans and procedures as needed.

Physical access mechanisms are in place to secure entry into CDC buildings (such as guards, ID badges/keycards, cipher locks, closed circuit TV).

All CDC users are required to complete annual Security Awareness and Privacy training before gaining access to CDC IT resources. All data access is protected using Personal Identity Verification (PIV) cards and/or complex passwords. At CDC, only Green Housing Study investigators will be given access to the data, implementing the least privilege method (only people whose jobs require access to the data are granted access).

CDC Green Housing Study investigators will receive electronic files with date of birth, medical information, biological specimens, employment status, and home address, identified by study ID number. While we acknowledge that home address is a unique identifier and the grantee will have the link to names and address, CDC Green Housing Study investigators are taking steps described in the previous paragraph to reduce the amount of individually-identifiable data maintained at CDC. If there were a breach of confidentiality for any of the above IIF, some effect on the respondent's privacy could occur; however, the screening form will be the only

form that contains name, home address, phone number, e-mail address, and study ID together; only the contracted data collectors will have this form. The contracted data collectors will only use name, phone number, e-mail address, and home address for locating the study participant and ensuring that follow-up questionnaires and clinical and environmental measurements are repeated accordingly. Contracted data collectors will be required to have human subjects training in accordance with their institution's Institutional Review Board (IRB) and/or the CDC's IRB. A component of human subjects training addresses data security measures.

A.3. Use of Improved Information Technology and Burden Reduction

Most of the data collection (i.e., 93%) from the study participants (i.e., the respondents) will be via paper forms; however, we are implementing text messaging to aid in monthly assessment of respiratory infections (i.e., 7% of data collection efforts). For the paper forms, the respondents will have minimal burden in providing their responses because they will not need to read questions nor write answers; the paid data collection grantee will record all of their verbal responses. The data collection grantee will then enter the survey data into an electronic database which will enable electronic transmission of data to CDC's Green Housing Study researchers. We chose paper forms for most of the data collection because at this time, it is the least expensive method (as opposed to transcribing answers from voice recorders or paying for laptop/ notepad computers). The text messages given at months 1, 2, 4, 5, 7, 8, 10, and 11 will only take approximately 1 minute to respond to a few brief questions of respiratory infections, and they can be answered at the respondents' convenience rather than relying upon direct interaction with the study team. We believe that this is an improvement over previous asthma studies that have relied upon a greater time period of recall between assessments.

A.4. Efforts to Identify Duplication and Use of Similar Information

CDC approached this in two ways: 1) we conducted a thorough literature search on green housing and health effects, and 2) we contacted subject matter experts from many different federal government agencies and private research organizations. In our literature search, we found that many studies had focused on relationships between housing characteristics and asthma, but none had specifically focused on how green housing factors were associated with these outcomes. The subject matter experts confirmed that a comprehensive evaluation of green housing factors and these health outcomes would be a novel and innovative approach to filling research gaps. The list of subject matter experts is listed in section A.8.

A.5. Impact on Small Businesses or Other Small Entities

The collection of this information does not directly impact small businesses or small entities.

A.6. Consequences of Collecting the Information Less Frequently

Some of the environmental and health outcome data are collected repeatedly (e.g., monthly, every 3 months or every 6 months) for several reasons: 1) to address seasonal variation in measurements; 2) to obtain better estimates of average exposure and/ or symptoms; and 3) to minimize recall bias. The technical obstacle to reducing the burden is as follows:

**Appendix C (The IRB-approved Protocol)**

If we do not obtain valid estimates of exposure and health effects, then it will be difficult to accurately attribute any reduction in exposure and improvement in health to specific green practices and/or materials.

There are no legal obstacles to reducing the burden.

A.7 Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

This request fully complies with the regulation 5 CFR 1320.5.

A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A. The text of the Federal Register notice for this information collection, published in *Federal Register* Volume 75, Number 22, on February 3, 2010, is provided in Appendix B. One public comment was received in response to that notice and it is attached as Appendix C. No change occurred in response to this comment because the comment was only a request for the data collection plans which were then provided to the requestor.

B. During the design phase of the this study, CDC's NCEH Healthy Homes and Lead Poisoning Prevention Branch reviewed published literature on green housing, and asthma and included consultation with researchers from HUD, EPA, other CDC branches (Division of Laboratory Sciences, Air Pollution and Respiratory Health Branch), and academic institutions. We have discussed availability of data and frequency of collection issues with subject matter experts (Table 12).

**Appendix C (The IRB-approved Protocol)**

Table 12. List of experts consulted regarding study design and frequency of data collection

| Name | Title | Affiliation | Contact information | Year of Consultation |
|---|---|---|---|---|
| Peter Ashley, DrPH | Director, Policy and Standards Division | U.S. Dept. of Housing and Urban Development | Peter.J.Ashley@hud.gov<br>Phone: 202-402-7595 | 2011 |
| Karen Bradham, PhD | Physical Scientist | U.S. Environmental Protection Agency | bradham.karen@epa.gov<br>Phone: 919-541-9414 | 2009 |
| Daniel Stout, PhD | Biological Scientist | U.S. Environmental Protection Agency | stout.dan@epa.gov<br>Phone:919-541-5767 | 2009 |
| Warren Friedman, PhD | Senior Advisor to the Director | U.S. Dept. of Housing and Urban Development | Warren.Friedman@hud.gov<br>Phone: 202-549-7868 | 2009 |
| Dana Barr, PhD | Branch Chief (Pesticide Laboratory) | CDC/NCEH/DLS* | Dlb1@cdc.gov<br>Phone: 770-488-7886 | 2009 |
| Benjamin Blount, PhD | Branch Chief (VOC and Perchlorate Laboratory) | CDC/NCEH/DLS* | Bkb3@cdc.gov<br>Phone: 770-488-7894 | 2009 |
| John (Thomas) Bernert, PhD | Branch Chief (Tobacco Exposure Biomarkers Section) | CDC/NCEH/DLS* | jtb2@cdc.gov<br>Phone: 770-488-7911 | 2009 |
| Fuyuen Yip, PhD | Team Lead | CDC/NCEH/ APHRB (Air Pollution and Respiratory Health Branch) | Fay1@cdc.gov<br>Phone: 770-488-3719 | 2008 |
| David Balshaw, PhD | Project Scientist | NIH, NIEHS | David.balshaw@nih.gov<br>Phone: 919-541-2448 | 2010 |
| Sung-Roul Kim | Research Associate | Johns Hopkins University | sung.r.kim@gmail.com<br>Phone: 011-82-2-380-7685 | 2009 |
| Mark Mendell, PhD | Staff Scientist | Lawrence Berkeley National Laboratory | mjmendell@lbl.gov<br>Phone: 510-486-5762 | 2009 |
| Brett Singer, PhD | Staff Scientist | Lawrence Berkeley National Laboratory | bcsinger@lbl.gov<br>Phone: 510-486-4779 | 2009 |
| Kim Dietrich, PhD | Professor | Univ. of Cincinnati | Dietrikn@ucmail.uc.edu<br>Phone: 513-558-0531 | 2009 |
| Gary Adamkiewicz, PhD | Research Scientist | Harvard School of Public Health | GADAMKIE@hsph.harvard.edu | 2008 |

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|---|---|---|---|---|
| | | | Phone: 617-384-8852 | |
| Wanda Phipatanakul | Assistant Professor | Harvard Medical School | Wanda.Phipatanakul@childrens.harvard.edu Phone: 617-355-6117 | 2008 |
| Robin Whyatt, DrPH | Professor | Columbia University | Rmw5@columbia.edu Phone: 646-459-9609 | 2008 |
| Andrew Gelman, PhD | Professor of Statistics | Columbia University | Gelman@stat.columbia.edu Phone: 212-851-2142 | 2008 |
| Elizabeth Matsui, MD | Associate Professor | Johns Hopkins University | ematsui@jhmi.edu Phone: 410-955-5883 | 2010 |
| Patrick Breysse, PhD | Professor | Johns Hopkins School of Public Health | pbreysse@jhsph.edu Phone: 410-955-3608 | 2010 |
| Jeanne Moorman, MS | Statistician | CDC/NCEH/ APHRB | zva9@cdc.gov Phone:770-488-3726 | 2011 |
| Herman Mitchell, PhD | Vice President & Senior Research Scientist | Rho Federal Systems Division | hmitchell@rhoworld.com Phone: 919-408-8000 x 6223 | 2011 |
| Lara Akinbami, MD | Commander, U.S. Public Health Service | CDC, National Center for Health Statistics | Lea8@cdc.gov Phone: 301-458-4306 | 2011 |

*CDC/NCEH/DLS = CDC, National Center for Environmental Health, Division of Laboratory Sciences

A.9 Explanation of Any Payment or Gift to Respondents

Study participants (mothers/primary caregivers of children enrolled in study) will receive compensation (see Table 13) for their participation in the study and to successfully increase response rates. Many of the low-income families in the proposed cohort use “pay-as-you-go” cell phones. The Green Housing Study team researched several calling card providers and found that they range in costs. For example, one company offers pre-paid plans at 25 cents a minute and another for 60 minutes at $19.99. For this reason, compensation for the text messaging and phone calls will be provided to help defray the costs to the participants.

Table 13. Monetary compensation for study participants

| Type of activity | Time point | Description of activities/ information/samples collected | Time | Amount of money |
|---|---|---|---|---|
| Home visit | - Baseline | Explanation of the study (includes informed consent process), blood sample, urine sample, lung function test, lung inflammation test, questionnaire, and environmental sampling in home* | 60 minutes | $50 |
| | - Baseline part 2 | urine sample, lung function test, lung inflammation test, questionnaire, and environmental sampling in home* | 55 minutes | $50 |
| | - 6 month follow-up | urine sample, lung function test, lung inflammation test, questionnaire, and environmental sampling in home* | 55 minutes | $50 |
| | -12 month follow-up | urine sample, lung function test, lung inflammation test, questionnaire, and environmental sampling in home* | 55 minutes | $50 |
| Phone calls | - 3 months<br>- 9 months | questionnaire | 5 minutes<br>5 minutes | $2<br>$2 |
| Text messages | - 1, 2, 4, 5, 7, 8, 10, and 11 months | Questionnaire. Each month, a series of 3 1-sentence texts will be sent to obtain this information, and the respondents will reply with 3 separate texts. | 1 minute for each month | $2 each time (maximum = $16) |

*This time indicates the amount of time required for setting up the environmental sampling equipment. Some environmental sampling equipment will be left in home for 5 days, but will not require any supervision.

Each study site will likely have certain rules about how money can be disbursed to the participants. We would like to use a relatively new method which is a pre-paid credit card (e.g., VISA, MasterCard) which can enable the following:

1. One card can be given to each enrollee's mother/primary caregiver at the beginning of the study.
2. The mother/primary caregiver will sign one receipt (at the beginning of the study) which acknowledges that the card will be uploaded with funds automatically (via a study site project coordinator) upon completion of each activity.
3. If the card is lost or stolen, the mothers/ primary caregivers can call the project coordinator who can cancel the card online. However, any funds that were missing from the lost or stolen card (prior to cancellation) will not be replaced. Only new funds will be added upon

completion of each of the remaining study activities listed in the incentive table. The mother/primary caregiver will receive the replacement card at the next home visit.

Rather than using checks or cash, this option will enable immediate payment especially for phone call questionnaires, reduce number of receipts, minimize danger of study staff carrying large sums of money to home visits, improve accounting, eliminate the need for low-income participants to pay check cashing fees, and ensure that the study participant retains our study phone number (which will be written on back of card).

In Table 14, the results of the review of federal national household interview surveys are shown. In these studies, the incentive ranges from $140 to $230. Many of these studies involve medical examinations and blood/urine sampling.

Table 14. Burden, Incentive, and Response Rates in Federal Studies with Multiple Data Collection Formats

| Study Name/Agency | Year | Study description | Respondent burden | Incentive | Response rate |
|---|---|---|---|---|---|
| Third National Health and Nutrition Examination Survey (NHANES III)/ CDC NCHS | 1988-1994 | NHANES is designed to collect information about the health and diet of people in the United States to provide current statistical data on the amount, distribution, and effects of illness and disability in the United States. | In-person interview, medical examination | $230 (plus exam results) | Interview=82% Exam=73% |
| National Human Exposure Assessment Survey (NHEXAS) Region 5/ EPA | 1995-1997 | A population-based pilot study of the exposure to metals, pesticides, volatile organic compounds, and other toxic chemicals of ~500 people in 3 US regions. | Questionnaires, video-taped observations, duplicate diet samples, collection of blood and urine, measurements of air quality and soil and dust in and around the home | $195 | Questionnaire = 71.5% Visit 1 = 80% Visit 2 = 56.8% Visit 3 = 47.8% |
| Minnesota Children's Pesticide Exposure Study (MNCPES)/ EPA | 1997 | Study of multi-pathway and multi-pesticide exposures in children. The primary objective was to characterize children's exposure to selected pesticides through a combination of questionnaires, personal exposure measurements and monitoring of biological samples, | 4-day duplicate diet samples, 6-days of personal air monitoring, keeping time and activity diaries, blood, urine and hair collections, videotaping. | $195 (children given age-appropriate gifts and parents offered videotapes of their children) | Telephone Screening = 67.5% |

| | | | | | |
|---|---|---|---|---|---|
| | | environmental samples, and children's activity patterns. | | | |
| School Health Initiative: Environment, Learning, Disease Study (SHIELD)/ EPA | 1999 | School-based investigation of children's environmental health in economically disadvantaged urban neighborhoods of Minneapolis. | Health questionnaires, 48-hour VOC sampling, blood draw, vacuum sampling in home, urine collections, school records review | $140 (children given age-appropriate gifts) | Recruitment= 56.7% (interviews/data collections ranged from 76-88%) |
| Biologic Specimen-based Study of Dietary Measurement Error/ NCI | 1999 | This study assessed dietary measurement error by comparing energy and protein intakes from two self-reported dietary data collection instruments (the NCI Diet History Questionnaire and the in-person 24-hour dietary recall interview) with two biomarkers (doubly labeled water and urinary nitrogen excretion) | Three clinic visits. Dietary History Questionnaire, 24-hour dietary recall, height/weight measurements, physical activity questionnaires, urine collection, Doubly-labeled water dose, 24-hour urine collection | $200 | Telephone recruitment=79 % Visit=100% (5 and 2 hours) |

A.10 Assurance of Confidentiality Provided to Respondents

Privacy Impact Assessment Information

A. This submission has been reviewed by ICRO, who determined that the Privacy Act does apply. The applicable System of Records Notice is 09-20-0136, Epidemiologic Studies and Surveillance of Disease Problems. While full names will not be sent to CDC, the grantee will have the capability of maintaining the link between name and study ID number; therefore, the privacy act does apply.

B. The Green Housing study staff (CDC and grantee) will make every effort to keep the data secure by a variety of methods. Data from paper questionnaires will be entered by the contracted data collectors into a database (e.g., Microsoft Access) which will be password-protected. Dates of birth and home addresses are primary direct identifiers and the grantee's removal of other direct identifiers (such as name, phone numbers, e-mail addresses) will minimize identification but not completely eliminate it. A unique Study ID will be assigned by the grantee as a key identifier for all study forms. The environmental and biological samples and measurements will only be identified by study ID. The removal of these identifiers will help to minimize, but not completely eliminate, the ability to identify individual participants. Contracted data collectors will maintain their paper files in locked cabinets and their electronic files will be stored on secured servers with password protection. Encrypted data files will be sent electronically to

Green Housing Study investigators at CDC. Data will be stored on highly-secured CDC servers in Atlanta, GA. The servers are housed in a secure computer room complete with climate control, emergency power, and an uninterruptible power supply (UPS). Daily back-ups and integrated security are implemented through the CDC computer services infrastructure. All data access is password-protected, and all network communications use encryption. All servers and PCs that are part of the CDC infrastructure are protected by both host-based firewalls and software in order to prevent the undetected installation of "spyware". At CDC, only Green Housing Study investigators will be given access to read the encrypted data files. CDC Green Housing Study investigators will receive electronic files with date of birth, medical information, biological specimens, employment status, and home address, identified by study ID number. While we acknowledge that home address is a unique identifier and the grantee will have the link to names and address, CDC Green Housing Study investigators are taking steps as described above in order to reduce the amount of individually-identifiable data maintained at CDC. If there were a breach of confidentiality for any of the above IIF at CDC, some effect on the respondent's privacy could occur; however, all health and exposure information from questionnaires will only be identified by study ID. The screening form will be the only form that contains name, home address, phone number, e-mail address, and study ID together; only the contracted data collectors will have this form which will be filed in their locked cabinets and stored in their password-protected database.

C. After discussions with some housing tenant's organization members and property managers, flyers (see Appendix H for a prototype of a recruitment flyer) were suggested as the optimal way to describe the study to the residents. Residents who express interest in the study can contact the site projector coordinator by telephone or e-mail. Subsequently, contracted staff (trained by CDC study investigators) will schedule a home visit with the residents. During this home visit, bilingual (English/Spanish or English/Chinese) study staff will describe the study again to the potential study participant. During this home visit, each resident's eligibility will be assessed (i.e. the Screening Form will be filled out by the aforementioned staff based on responses from the mother/ primary caregiver). If a resident is eligible and is willing to participate, then the individual consent (or assent) form will be reviewed with the study participant in language (English, Spanish, or Chinese) appropriate to participant. If the resident agrees to participate, the consent form will be signed by both the participant and the interviewer obtaining consent. The consent form (Appendix F) describes the purpose of the study, what is expected of the participant during the study, intended uses of the data, study duration, alternatives to participation, data security and data sharing, compensation, and potential risks and benefits of the study. During the consent process, potential subjects are encouraged to ask questions. Participation in the study is voluntary, and withdrawal from the study has no influence on future healthcare. Assent will be obtained from children age 7-12. The assent form (Appendix G) is a simplified version of the consent form that is written at a level that a child (age 7-12) can understand and they are encouraged to ask any questions they might have about the study. The children ages 7-12 will be assenting to providing blood and urine samples for the study; they will <u>not</u> be asked to respond to survey questions—enrollees' mothers/ primary caregivers will be providing that information. Copies of the consent and/or assent forms will be provided to the study participants. Contracted data

collectors will be required to have human subjects training in accordance with their institution's Institutional Review Board (IRB) and/or the CDC's IRB. A component of human subjects training addresses data security measures.

D. During the consent process, CDC-trained interviewers will explain to the residents that participation in the study is voluntary and they may withdraw from the study at any time without negative consequences. The interviewers will also explain the intended uses of the data (i.e., to study how green housing affects respiratory outcomes), with whom information will be shared (i.e., Green Housing Study researchers), and the legal authority for the data collection (i.e., through the Public Health Service Act).

This study was originally approved by the CDC's IRB (protocol #5587) on March 30, 2009 and then received a continuation on March 26, 2010 (Appendix E).

Data will be treated in a secure manner and will not be disclosed, unless otherwise compelled by law. The Information in Identifiable Form (IIF) collected during the course of the Green Housing Study is listed in section in Table 15. As described earlier Table 9 also describes the IIF, its intended uses, and who will have access to the IIF.

Table 15. Information in Identifiable Form (IIF) and intended uses

| IIF category | Collected by grantee but not sent to CDC | Collected by grantee and sent to Green Housing Study staff at CDC | Purpose |
|---|---|---|---|
| name | X | | Names are required for written informed consent. In addition, names aid both the study participant and the data collector during in-person and telephone questioning. |
| date of birth | | X | To determine eligibility and to also adjust for age in statistical analysis. |
| phone numbers | X | | To administer phone questionnaires. |
| medical information and notes | | X | To assess health outcomes for statistical analysis |
| biological specimens | | X | To assess health-related biomarkers for statistical analysis |
| e-mail address | X | | To serve as a secondary means of contacting study participants to administer questionnaires and schedule home visits for sampling |
| employment status | | X | To adjust for possible chemical exposures that could occur in the occupational environment. |
| home address | | X | To enable grantee to visit homes for sampling and also enable CDC to use geographic information systems (GIS) which can be used for adjusting for factors external to the home which could influence both exposures and health outcomes (e.g., outdoor air pollution). |

## A.11 Justification for Sensitive Questions

Several questions in the questionnaires ask for information that could be considered sensitive by at least a segment of the general population (Table 16), but variables such as smoking and presence of cockroaches, mice, and rats are specifically geared toward factors that could be related to respiratory health. These items are necessary to assess the relationship between the presence of environmental exposures and the residents' health (Chew et al., 1998). A copy of the questionnaires can be found in Appendix D (D1-D12). The interviewers are given detailed instructions within each of the questionnaires on how to collect the information, including skip patterns and when to probe for certain questions (e.g., types of inhaled corticosteroid medications typically used by the child with asthma). Interviewers will also be trained to be sensitive to any questions likely to cause discomfort, and the respondent will be informed of her right to refuse to answer any interview question.

Table 16. Questions of a possibly sensitive nature

| Questions (possibly sensitive) | Specific uses of information |
|---|---|
| | |
| Which one or more of the following would you say is your race? | To adjust for race in statistical models. |
| What is the highest level of school that you have completed or the highest degree that you have received? | To adjust for socioeconomic status in statistical models. |
| Which category represents the total combined income of all members of this family during the past 12 months? | To adjust for socioeconomic status in statistical models. |
| Do you smoke cigarettes? | To adjust for smoking exposure in statistical models. Smoking could affect our environmental and clinical measurements. |
| During the past 6 months, how often have you seen cockroaches in your household? | To assess cockroach exposures pre- and post- interventions. |
| During the past 6 months, how often have you seen mice in your household? | To assess mouse exposures pre- and post-interventions. |
| During the past 6 months, how often have you seen rats in your household? | To assess rat exposures pre- and post-interventions. |

Explanation given to respondents: These questions are needed for this study and some of them have been shown to be associated with environmental exposures and health outcomes, so we need to take them into account.

A.12 Estimates of Annualized Burden Hours and Costs

A. As discussed in the Background section of this ICR, we hypothesize that children ages 7-12 with asthma who live in green housing, will have improved health outcomes as compared to those who live in comparison housing. Consequently, the respondents that will complete the questionnaires are mothers/ primary caregivers of enrolled children with asthma (ages 7-12 years).

Approximately 1000 adults will complete the screening forms. Kass et al. (2009) obtained a screening percentage of 73% in their New York City Housing Authority intervention study. We estimate that after screening, 20% of households will not be eligible.

Two large-scale housing intervention studies in low-income neighborhoods that had a 1-year follow-up have reported response rates of 92-93% (Morgan et al., 2004; Persky et al., 2009). With an anticipated loss to follow-up in our study of 20%, we will recruit 832 households with asthmatic children to end up with 650 enrolled children with asthma (ages 7-12 years) . All health and environmental exposure information about children will be provided by their mothers/ primary caregivers (i.e., no children will fill out questionnaires). For the purposes of assessing potential burden, we are using the maximum of 832 mothers/ primary caregivers

who could conceivably fill out the forms. The burden hours for each type of respondent are listed below in Table 17.

Each of the questionnaires was pilot-tested at CDC on nine predominantly college-educated CDC employee-volunteers during non-work hours. The pilot tests were administered by two Green Housing Study researchers. The results of our pilot testing are shown in Part B, Table 25. Based upon pilot testing, the questionnaires were revised to increase ease of understanding and speed of response. We conservatively estimated of the response times for our study participants (low-income mothers/ primary caregivers living in multifamily, urban housing) based on the average response times recorded during our pilot tests.

Table 17. Estimated Annualized Burden Hours

| Forms | Respondents | No. of Respondents | No. of Responses per Respondent | Average Burden per Response (in hours) | Total Burden (in hours) |
|---|---|---|---|---|---|
| Screening questionnaire | Mothers/ primary caregivers of children with asthma | 1000 | 1 | 10/60 | 167 |
| Baseline Questionnaire (Home Characteristics) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 15/60 | 208 |
| Baseline Part 2 Questionnaire (Home Characteristics) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 5/60 | 69 |
| Baseline Questionnaire (Demographics) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 5/60 | 69 |
| Baseline Questionnaire (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 15/60 | 208 |
| Monthly texts | Mothers/ primary caregivers of enrolled children | 832 | 8 | 1/60 | 111 |
| 3 and 9-month Phone contact | Mothers/ primary caregivers of enrolled children | 832 | 2 | 5/60 | 139 |
| 6 and 12-month Follow-up Questionnaire (for environment) | Mothers/ primary caregivers of enrolled children | 832 | 2 | 10/60 | 277 |

| | | | | | |
|---|---|---|---|---|---|
| 6 and 12-month Follow-up Questionnaire (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 2 | 10/60 | 277 |
| Time/Activity form (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 4 | 5/60 | 277 |
| Time/Activity form (for mothers/ primary caregivers) | Mothers/ primary caregivers of enrolled children | 832 | 4 | 5/60 | 277 |
| Illness Checklist | Mothers/ primary caregivers of enrolled children | 832 | 4 | 5/60 | 277 |
| Maximum number of respondents 1000 | | | Total estimated burden hours 2,356 | | |

B. We assumed earning potential for participants in our study (low-income mothers/ primary caregivers living in multifamily, urban housing) was minimum wage (as of May 11, 2011, the Federal minimum wage was $7.25 per hour (http://www.dol.gov/dol/topic/wages/minimumwage.htm) based on data provide by HUD regarding income of public housing residents (HUD 2009). From December 01, 2008 through March 31, 2010, the average income of residents living in public housing was $13,414 and 72% of the residents reported an income of $15,000 or less. For our study, we selected a conservative estimate of annualized burden cost (i.e., $7.25 per hour for one year of employment = $15,080). Therefore, the true annualized burden could be lower than the estimates in Table 18.

Table 18. Estimated Annualized Burden Costs

| Forms | Respondents | No. of Respondents | No. of Responses per Respondent | Average Burden per Response (in hours) | Total Burden (in hours) | Hourly Wage | Total Respondent Costs |
|---|---|---|---|---|---|---|---|
| Screening questionnaire | Mothers/ primary caregivers of children with asthma | 1000 | 1 | 10/60 | 167 | $7.25 | $1210.75 |
| Baseline Questionnaire (Home | Mothers/ primary caregivers | 832 | 1 | 15/60 | 208 | $7.25 | $1508 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Characteristics) | of enrolled children | | | | | | |
| Baseline Part 2 Questionnaire (Home Characteristics) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 5/60 | 69 | $7.25 | $500.25 |
| Baseline Questionnaire (for Mother/ primary caregiver) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 5/60 | 69 | $7.25 | $500.25 |
| Baseline Questionnaire (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 1 | 15/60 | 208 | $7.25 | $1508 |
| Monthly texts | Mothers/ primary caregivers of enrolled children | 832 | 8 | 1/60 | 111 | $7.25 | $804.75 |
| 3 and 9-month Phone contact | Mothers/ primary caregivers of enrolled children | 832 | 2 | 5/60 | 139 | $7.25 | $1007.75 |
| 6 and 12-month Follow-up Questionnaire (for environment) | Mothers/ primary caregivers of enrolled children | 832 | 2 | 10/60 | 277 | $7.25 | $2008.25 |
| 6 and 12-month Follow-up Questionnaire (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 2 | 10/60 | 277 | $7.25 | $2008.25 |
| Time/Activity form (for Children with asthma 7-12 years) | Mothers/ primary caregivers of enrolled children | 832 | 4 | 5/60 | 277 | $7.25 | $2008.25 |
| Time/Activity form (for mothers/ primary | Mothers/ primary caregivers of | 832 | 4 | 5/60 | 277 | $7.25 | $2008.25 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| caregivers) | enrolled children | | | | | | |
| Illness Checklist | Mothers/ primary caregivers of enrolled children | 832 | 4 | 5/60 | 277 | $7.25 | $2008.25 |
| | | | | | | Total = | $17,081.00 |

A.13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There is no anticipated cost burden to respondents resulting from the collection of information, except the costs associated with the respondents' time. Respondents will not be required to incur (a) capital or start-up costs; or (b) operation and maintenance and purchase of services costs. Respondents will not be asked or required to keep any records.

A.14. Annualized Cost to the Government

The Green Housing Study will be conducted by CDC and grantee to be determined (TBD) via Inter-agency agreement (IAA) with HUD (#I-PHI-01062) (i.e., HUD will transfer the funds to CDC). The IAA with HUD is for 5-years, although we acknowledge that we can only apply for OMB approval for a 3-year period. Prior to the expiration of the initial 3-year OMB approval, we will file for a renewal.

The IAA for the 5-year study allots costs of $2,000,000 for subcontracting of the TBD staff, travel, interviewing, supplies, sample collection, laboratory analyses, data analysis, and reporting. The estimated cost for CDC personnel, study coordination, laboratory analysis, data analysis and oversight of the grantee's work is $1,190,000 over a 5 yr period (Table 19 shows the annual costs). Another Federal Agency, HUD, will devote personnel, data interpretation, and travel, at a cost of $50,000, over the approximate 5-year period. The estimated total cost for the Green Housing Study is approximately $3,240,000, over the 5-year period.

Table 19. Overall Cost Estimate of Proposed Study

| Category | Annual Costs (dollars) |
|---|---|
| CDC, including | Total = $238,000 |
| -three staff (GS-13) at 75% effort | $225,000 |
| - travel for site visits | $13,000 |
| HUD, including one staff (GS-14) and travel to Atlanta's CDC office | $10,000 |
| TBD grantee, including all staff, travel, interviewing, supplies, sample collection, laboratory analyses, data analysis, and reporting | $400,000 |
| Total costs | $648,000 |

A. 15. Explanation for Program Changes or Adjustments

This is a new data collection.

A.16. Plans for Tabulation and Publication and Project Time Schedule

Reports associated with the study will include reports for respiratory outcomes. In addition to those reports, CDC will prepare at least three peer-reviewed journal articles of respiratory outcomes. CDC will also provide technical information and recommendations to various housing programs based on the findings of this study.

The research program will be conducted over a period of 5 years; however OMB clearance is being requested for 3 years. Prior to expiration of OMB clearance, Green Housing Study researchers will submit required documents to OMB in support of a renewal request. Table 20 shows the projected schedule of accomplishments and milestones for the study. Note, items in the table that will occur after the original OMB clearance period are noted with an asterisk; these items are scheduled to occur after the initial 3-year period and therefore will be predicated upon obtaining a renewal for OMB clearance.

Table 20. Project Time Schedule

| Activity | Months after OMB approval |
|---|---|
| Select at least two study sites (with help of HUD) | 1 |
| Subcontract the collection of data to the local study sites. | 1 |
| Train study staff from each site to collect environmental, survey, and clinical data | 1 |
| Data collection | 2 |
| Subcontract with laboratories to assay environmental samples and biomarkers collected during the study. | 2 |
| Summary of laboratory results from subcontracted institutions | 6, 12, 24, 36, 48*, 60* |
| Summary of survey results from study sites | 6, 12, 24, 36, 48*, 60* |
| Conduct statistical analysis | 6, 12, 18, 24, 30, 36, 42*, 48*, 52*,60* |
| Forms used for reporting study results back to participants and community | 6, 12, 60* |
| Quarterly reporting: Provide draft quarterly reports within 21 days after the end of the quarter, which HUD shall review and comments within 10 days after receipt; and provide the quarterly report, within 7 days after receipt of HUD comments | 4,7,10,13,16,19,22,25,28,31,34, 37*,40*,43*,46*,49*, 52*, 55*, 58* |
| Submit articles for peer review in journals | 12, 24, 36, 60* |
| Final: Provide draft quarterly reports within 90 days after the end of the study, which HUD shall review and comments within 30 days after receipt; and provide the final report, within 21 days after receipt of HUD comments | 60* |

*Asterisked items are included here for completeness since much of the data analysis and dissemination of study findings will occur after the initial 3-year OMB approval timeframe.

The analysis plan includes the following: 1) descriptive statistics to show prevalence of environmental exposures and health outcomes (i.e., asthma morbidity) and 2) logistic and linear regressions to examine associations between environmental exposures such as indoor allergens, mold, pesticides, and VOCs and health outcomes. Detailed statistical analyses are described in section B.

A.17. Reason(s) Display of OMB Expiration Date is Inappropriate

The selection of study sites across the country will occur on a rolling basis over the course of the study. At each study site, contracted data collectors will collect data using CDC's OMB-approved questionnaires. It is conceivable that data collection at one or more study sites will start or be continued from one OMB approval to the next. Consequently, to avoid the necessity

of reprinting forms (with the new OMB expiration date), and thereby wasting paper, we request that the expiration date not be printed on the questionnaires.

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

**Appendix C (The IRB-approved Protocol)**

# The Green Housing Study

## Supporting Statement

## (Part B)

October 20, 2011

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B. Collections of Information Employing Statistical Methods

## B.1. RESPONDENT UNIVERSE AND SAMPLING METHODS

The purpose of this study is to provide insight into the potential implications of green renovations for the health of young asthmatics who live multifamily HUD-subsidized housing in the United States and U.S. territories. According to HUD, 970,532 households live in public housing in the United States (HUD 2009). The number of M2M properties is in flux according to market forces and other factors such as landlord motivations for participation; however, it is estimated that since 1997, 1600 developments (with approximately 100 units each) have been renovated through the M2M Green Initiative http://www.hud.gov/offices/hsg/omhar/paes/greenini.cfm**.** Collecting data from asthmatic children in all housing units being renovated would be too burdensome, expensive, and logistically impractical. We will include a targeted non-probability sample of 832 homes in 13 cities for this study methodology. HUD had selected housing developments for green renovations projects prior to the inception of this proposed study based upon specific requirements (e.g., use of low VOC materials, use of energy efficient appliances). Figure 8 illustrates the sampling process. Since the housing developments were already selected based on grant awards, random assignment of the green intervention was not possible for this study.

The selection of the cities is based upon the following:

City must have one or more housing developments which are receiving a HUD-subsidized green-renovation. These renovations must occur within the timeline of our study period (5 years, although, we will ask OMB for a continuation prior to the expiration of the initial 3-year OMB approval). Housing developments should have many apartments which will undergo the green renovations. Smaller housing developments would severely hamper recruitment of our targeted sample size in each city. However, we will consider cities which have several housing developments with a smaller number of apartments, given that the housing developments will undergo renovations within 6 months of each other.

Green renovations must meet inclusion criteria: Low VOC materials and Integrated Pest management (IPM).

The housing renovations within the city must occur in areas with high prevalence (i.e., greater than the national average, currently 9.1%) of childhood asthma (based upon National Health Interview Survey data, (Akinbami et al., 2009)). This is to enhance the potential pool of study participants. Areas of lower asthma prevalence would severely hamper recruitment of our targeted sample size in each city.

Cities are located in different regions of the country and/or represent different types of housing stock.

The design being used allows us to provide insight into the societal benefits of green housing on low income families with asthmatic children. However, it will not be generalizable to respondents or even geographically or demographically defined subgroups due to the fact that

both the applicants of the HUD awards and the households themselves are self-selected. Specifically, the design does not allow generalizations based on city, type of locations (rural, suburban), climactic regions (e.g., desert, arctic), or ethnicities. Furthermore, this study will systematically exclude certain subsets of the population for logistical reasons. Specifically:

i. Public housing is comprised mostly of 3 main ethnicities: white, African-American, and Latino (HUD, 2009).

ii. Our main health endpoint, asthma, is highest among Latinos and African-Americans. While several childhood asthma studies have focused on some minority populations in the United States (African American and Latino), only recently have investigators focused studies of Asian populations. In the Boston Chinatown neighborhood, researchers found a higher prevalence of asthma for children born in the US as compared to those who were foreign-born in an Asian population, enriched with recent Chinese immigrants (Brugge et al., 2007). These results confirm findings in a similar Asian population from the same community (Greenfield et al., 2005).

iii. We do not have the capacity to translate into all languages. However, we determined that it would be beneficial to include Spanish and Chinese translations for the reasons mentioned above. In meetings with stakeholders at our first potential study site, Boston, we found that they have a substantial Chinese population (along with Latino and African-American). The tenants' organization asked if we would recruit the Chinese residents too and if we could translate all of our materials into Chinese. We believe that the tenants' organization's request is reasonable. Furthermore, in other potential study site locations (e.g., Los Angeles, New York, San Francisco), Chinese language translation might also be relevant.

We assume an 80% participation rate for the eligible residents for the collection as a whole (as described in Part B, section 3).

The design is stratified by city. As discussed below, one pair of housing developments will be chosen in each of 13 cities that meet the criteria delineated in section B1. We will frequency match green intervention and comparison homes by HUD-subsidized housing development, asthma status of children, age group of asthmatic children (7-12 years) and primary language spoken by mother/primary caregiver of the asthmatic child. We are not matching on ethnicity *per se*; however, much of the low-income housing in inner-city communities tend to be segregated to some extent, by race/ethnicity (Acevedo-Garcia and Lochner 2003). We will record race/ethnicity in our questionnaire and adjust accordingly in our analysis. As mentioned earlier, this selection will be limited by the availability of the ongoing HUD renovation efforts. There are no other problems requiring specialized sampling procedures. The data collection plan requires only one series of data collection within a one-year follow-up period.

Sample size overviews: Our calculations estimate that 416 subjects/study arm (i.e., green vs. comparison homes) must be recruited in order to achieve sufficient statistical power to statistically differentiate between the study arms (this paragraph outlines the calculations supporting this estimate, with details in subsequent paragraphs of this section; see also figure below). In order to have sufficient power to detect meaningful differences in both environmental

measurements and health outcomes between the arms, we began by calculating sample sizes based on each of these measures.

Our sample calculations for environmental measurements (see Table 21) were based on cockroach allergen data in a repeated measures study of the effect of an integrated pest management (IPM) intervention, which indicate that 13 buildings would be necessary in each of the two arms of the study, assuming that 25 subjects could be recruited for each building, yielding 325 subjects/study arm to provide adequate statistical power for environmental measurements.

Our sample calculations for health outcomes (see Table 22) were based on asthma in children subjected to a multifactorial intervention (i.e., education, mattress covers, IPM, and HEPA filter units) in a repeated measures study. These data indicate that 274 subjects/study arm would be needed to provide adequate statistical power for asthma outcomes.

Therefore, since we desired sufficient power to detect meaningful differences in both 1) environmental measurements and 2) health outcomes, we selected the larger of the two estimates — 325 subjects/study arm — as the minimum sample size (see Figure 7). In addition, we augmented this number in order to account for an anticipated 20 percent loss to follow-up over a one-year period. After rounding up where necessary, this increased the sample size to 416 subjects/study arm, comprising 32 subjects (one subject per apartment) in each of 13 buildings in each study arm. The total sample size for the study across both study arms is 832 subjects. The details of our sample size calculations are listed below and the equations that were used were from a book on longitudinal data analysis by Diggle, Liang, and Zeger (1994).

Figure 7. Summary of sample size

Sample size calculations for the overall difference between environmental exposures in green vs. comparison homes can be given as a simple test of two proportions and means; however a specific difficulty arises when trying to adjust for temporal and spatial correlations between measurements. A study that had enough measurements to assess spatial and temporal correlation was an integrated pest management (IPM) study conducted in New York City (Chew et al., 2006; Kass et al., 2009). We have used the design effect from this study to estimate the number of clusters (or buildings) needed to detect differences in cockroach allergen because IPM is also one of the main green characteristics in the Green Housing Study. Assumptions from the aforementioned study comparing IPM to non-IPM homes are listed below:

13 buildings

About half were treatment and the other half comparison

3 repeated measures at: baseline (before IPM), 3months later (post-IPM), and 6months later (post-IPM)

On average, 25 apartments within each building were measured

For the comparison homes, the correlations between baseline and 3-month follow-up cockroach allergen measurements and 3-month and 6 months follow-up measurements were approximately equal to 0.5.

Design effect due to clustering = 3.62

Equation 1. Sample size for repeated measures – cockroach allergen.

$$m = D * [2(z_{\alpha} + z_{Q})^{2}\{1 + (n-1)\rho\}]/(n\Delta^{2})$$

m = number in each group (e.g., intervention and non-intervention)
n = number of repeated measurements (equals 3 in this scenario)
$z_{\alpha}$ = Z score for alpha = 0.05
$z_{Q}$ = Power, set at 0.80
ρ = correlation among repeated observations
Δ = d/ σ where d is the smallest meaningful difference and σ is the standard deviation
D = Design effect due to clustering of apartments within buildings (This was not in the formula used by Diggle et al. (1994), but was added to adjust for clustering expected in our study.)

Note: we also assumed a design effect (e.g., increase (multiplicative) sample needed because of the effects of clustering) equal to 3.62. This is the ratio in clustering sampling variance divided by the simple random variance (of the same size) (i.e., the denominator without clustering taken into account).

When calculating the sample sizes, we used two standardized effect sizes based on the IPM study: 0.37 and 0.30. The effect size of 0.37 is based on the ability to detect a difference of 0.8148 ln units of the *Blatella germanica* cockroach allergen (i.e., Bla g 2) and a standard deviation of ~ 2.2. The effect size of 0.30 is the based on the ability to detect a difference of 0.649 ln units of Bla g 2 and a standard deviation of 2.2. We also assumed an alpha of 0.05 and a power of 80%). The sample size based on changing the expected correlation between repeated measures would result is presented in Table 21.

Assuming a correlation of 0.5 we get the following:

With assumption 1, we would need 16 buildings (8 green and 8 comparison) with at least 25 apartments per building

With assumption 2, we would need 26 buildings (13 green and 13 comparison) with at least 25 apartments per building.

Table 21. Sample size requirements for number of buildings.

| Correlation between repeated measures | Sample size requirements (number of buildings) | |
|---|---|---|
| | Assuming Delta=0.377 | Assuming Delta=0.30 |
| 0.2 | 6 | 9 |
| 0.3 | 7 | 11 |
| 0.4 | 8 | 12 |
| 0.5 | 8 | 13 |
| 0.6 | 9 | 15 |
| 0.7 | 10 | 16 |
| 0.8 | 11 | 17 |

*sample size is for each group (e.g., 8 buildings means 8 comparison and 8 green buildings)

We also estimated the sample size for detecting differences in pesticides and VOCs. To date, there is only one study of an intervention to decrease pesticide exposures that used objective measurements of pesticide levels in residential homes in a non-agricultural environment (Williams et al., 2006). This study was conducted in homes of Latina and African-American women living in low-income housing in New York. In the study, 25 homes underwent IPM as an intervention. The pesticide synergist, piperonyl butoxide, is unique to pyrethoid pesticides and this was an analyte that was measured in the study's air samples. We used their pre- and post piperonyl butoxide concentrations (pre = mean 1.66 ± s.e. 0.71 ng/$m^3$ vs. post = mean 0.8 ± s.e. 0.22 ng/$m^3$) for our calculations of sample size which are shown in Table 22.

To date, there is only one study comparing the VOC levels in newly-built green homes and conventionally-built homes; therefore, this was not a renovation like our proposed study. We calculated the sample size based on their measurements of formaldehyde in the two types of homes in their study. This study was conducted in Finland. In the study, 6 apartments in each type of building had air measurements for formaldehyde (green-built: mean = 13 µg/$m^3$, s.d. = 4 vs. conventionally-built: mean 23 µg/$m^3$, s.d. = 5). We calculated the sample size necessary to detect a decrease in 50%, 25%, and 15%, of the difference in formaldehyde levels observed in their two study groups (see Table 22).

Devos et al. (1990) have suggested that the minimum level of an indoor irritant be set with a safety factor of 40 (Devos, Patte et al., 1990). Given that the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value is 368 µg/$m^3$, a minimum level of formaldehyde below which no irritant effects are expected is 9.8 µg/$m^3$ (which is the CDC/ATSDR Minimum Risk Level, http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=220&tid=39 ).

Table 22. Calculations of samples sizes for VOCs and pesticides

| Analyte | Design Effect | Effect Size (Δ) | Required Sample size (in each group) |
|---|---|---|---|
| Formaldehyde<br>- 15% : 1.5 μg/$m^3$<br>- 25% : 3.5 μg/$m^3$<br>- 50% : 5 μg/$m^3$<br><br>(based on Tuomainen et al., 2003) | <br>3.6<br>3.6<br>3.6 | <br>0.33<br>0.77<br>1.10 | <br>408<br>75<br>37 |
| Piperonyl butoxide<br>0.8 ng/$m^3$ decrease<br><br>(based on Williams et al., 2006) | 3.6 | 0.33 | 418 |

* α = 0.05, 1-β = 0.80

Summary of sample size for environmental exposures: Of the intervention studies relevant to green housing, the sample size calculations based upon the cockroach allergen intervention study provided the most information to inform our estimates of sample size required for the Green Housing Study. Because Dr. Chew was a co-author on the manuscript and had analyzed the cockroach allergen samples in her laboratory, she had access to the repeated measurements database and this helped to guide our design effect due to clustering of apartments within buildings. The other papers did not have repeated measurements (thus the variance estimates were rather wide) and they also had more restrictive groups (e.g., nonsmoking pregnant women, Finnish families living in newly-constructed apartments) than is planned in the Green Housing Study. Thus, we believe that our estimates are conservative.

Sample size for assessing asthma outcomes: The calculation for assessing differences in health markers were based upon a multi-site asthma intervention study (Morgan et al., 2004). In this study, 407 asthmatic children with the multi-factorial intervention (asthma trigger education, mattress covers, IPM, HEPA filter units) had fewer days (2.62 days ± 0.12) than those (n=414) without the intervention (3.21 days ± 0.13). Table 15 shows sample sizes with different assumptions of effect sizes using equation 2.

Equation 2. Sample size for asthma morbidity outcomes.

$$m = D * [2(z_\alpha + z_Q)^2\{1 + (n-1)\rho\}]/(n\Delta^2)$$

m = number in each group (e.g., intervention and non-intervention)
n = 1 (note: for differences of differences, we assumed a value of 1)
$z_\alpha$ = Z score for alpha = 0.05
$z_Q$ = Power, set at 0.80
ρ = correlation among repeated observations
Δ = d/ σ where d is the smallest meaningful difference and σ is the standard deviation
D = Design effect due to clustering within 13 sites (This was not in the formula used by Diggle et al. (1994), but was added to adjust for clustering expected in our study.) Based upon the Kwon et al. (2003) paper that showed a design effect of 1.5 was helpful for designing cluster

studies to assess asthma outcomes in national surveys (e.g., BRFSS and NHANES), we assumed a slightly smaller design effect equal 1.2 due to the expected low average number of children per cluster).

Table 23. Sample size requirements for number of children with asthma.

| Effect size (i.e., delta) | Sample size requirements (number of asthmatic children) | |
|---|---|---|
| | in Green buildings | in Comparison buildings |
| 0.20 | 274 | 274 |
| 0.232* | 274 | 274 |
| 0.30 | 206 | 206 |
| 0.35 | 151 | 151 |
| 0.40 | 116 | 116 |

* Based on observed effect size from Morgan et al. (2004) study.

We used Equation 3 to calculate the sample size based on binary outcomes. The assumptions for the equation were based upon an intervention study in Seattle Public housing (Krieger et al., 2005). The Seattle researchers had n= 110 in a high-intensity intervention group and n = 104 in a low-intensity intervention group follow. They assessed the percentage of children in each group with urgent health service use in the past 2 months. Taking the difference between baseline and exit measurements of the two proportions for high-intensity (23.4% - 8.4% = 15% difference) and low-intensity (20.2% - 16.4% = 3.8% difference), we calculated n= 102 in each study group.

Equation 3. Sample size for binary asthma morbidity outcomes.

$$m = [[(z_{\alpha}\{2\bar{p}\bar{q}\,(1+(n-1)\rho)\}^{\frac{1}{2}} + z_{Q}\{(1+(n-1)\rho)(p_{A}q_{A} + p_{B}q_{B})\}^{1/2}]^{2}]/nd^{2}$$

m = number in each group (e.g., intervention and non-intervention)
n = 1 (note: for differences of differences, we assumed a value of 1)
$z_{\alpha}$ = Z score for alpha = 0.05
$z_{Q}$ = Power, set at 0.80
ρ = correlation among repeated observations
$p_A$ = proportion of Group A
$p_B$ = proportion of Group B
$q_A$ = 1- proportion of Group A
$q_B$ = 1- proportion of Group B
$\bar{p} = \bar{p} =$ $(p_A + p_B)/2$
$\bar{q} = \bar{q} = 1 - \bar{p} 1 - \bar{p}$
d = is the smallest meaningful difference between proportions
D = Design effect due to clustering (This was not in the formula used by Diggle et al. (1994), but was added to adjust for clustering expected in our study.) Based upon the Kwon et al. paper (2003) that showed a design effect of 1.5 was helpful for designing cluster studies to assess asthma outcomes in national surveys (e.g., BRFSS and NHANES), we assumed a slightly smaller design effect equal 1.2 due to the expected low number of expected of average children per cluster).

B.2. Procedures for the Collection of Information

The characteristics of study participants that will be included are: 1) Children age 7-12 years with asthma (note: The child must have been diagnosed with asthma by a physician and have had asthma-related symptoms (wheezing, slow play or night awakening) during the past 6 months), and 2) mothers/ primary caregivers of enrolled children. Also, the mother/ primary caregiver must speak English, Spanish, or Chinese to be included in the study and the enrolled participants must live in the home (from which environmental samples will be collected) on average 7 days per week.

Upon notification from HUD that a participating housing complex is about to begin rehabilitation, CDC will contact local academic institutions and departments of health in order to mobilize the Green Housing Study in that location. We envision that together with HUD and local academic investigators at the selected sites, CDC will convene town meetings at each participating complex to describe the study to residents, answer questions, and invite their participation. Depending upon the number of residents who initially volunteer at the town hall, we will convene additional town hall meetings to augment participation. Residents who express interest in the study can contact the site projector coordinator either at the town hall meetings or by telephone. Subsequently, the trained staff will schedule a home visit with the residents. For quality control purposes, teams of two trained staff will visit the home to collect questionnaire data via an in-person interview and perform environmental sampling. The environmental sampling technician will review the questionnaire information that the other technician obtained during the interview with the study participant. Also, the database entry screen will have validation checks (e.g., number of reported asthma symptoms cannot equal a negative number)

Statistical analysis: The main variable of interest is the type of home (green vs. comparison); however, there may be different permutations within green housing. For example, HUD has two levels of green which are based upon the acceptance of HUD-approved recommendations: Level 1) landlord agrees to implement at least 75% of the dollar amount of green repairs and improvements; and Level 2) landlord agrees to implement at least 50% of the dollar amount. While discretizing the green rehabilitation into Level 1 and Level 2 categories could simplify our analysis, we acknowledge that the two different levels do not necessarily capture green materials or practices that are potentially related to health. For example, a green home could have low VOC paint, or low VOC carpet, or replace the kitchen cabinets with low VOC materials, or have some combination of these activities.

***Allergens in the homes: Variables related to indoor allergens in the homes may take the form of continuous measures of specific allergens or of indicator variables for the presence or absence of certain allergens or combinations of allergens. Allergen concentrations will be reported as μg of allergen per g of collected dust and μg of allergen per unit area vacuumed.***

***VOCs and pesticides in the homes: Variables related to VOCs (whether total or speciated) and pesticides (pyrethroids, propoxur, and piperonyl butoxide) in the homes may take the form of continuous measures or indicator variables for the presence or absence of certain chemicals or combinations of chemicals. Concentrations will be reported as ppm (and also μg/$m^3$) in the case of the VOCs and μg/g in the case of the pesticides.***

***<u>Conditions of the home environments</u>: Factors that may influence the presence and levels of allergens, VOCs, and pesticides include: the presence of carpets; pests; housing type and age, average winter temperature and relative humidity, air exchange rates.***

***<u>Wheeze /asthma severity</u>: This information may be used in the form of categorical and continuous variables (number of emergency room visits for asthma, use of asthma medications, lost school days). Nights awakened by asthma, and spirometry measurement such as FEV1 and $FEF_{25-75\%}$).***

***<u>Additional environmental and host factors for disposition to wheeze/asthma:</u> Other risk factors for the main outcomes of interest include: environmental tobacco smoke; acute respiratory illnesses; gender; socioeconomic status of primary caregiver; degree of acculturation (operationalized); and deficiencies in access to and quality of health care. Many of these factors allow for a variety of formulations. Environmental tobacco smoke, for example, may be analyzed as an indicator variable for the presence or absence of smoking in the home, as count data for the number of smokers in the home, or as a continuous variable for the number of cigarettes smoked per day in the home. The choice of formulation of risk factors will be driven by the aim of clarifying the main relationships of interest, for example the role of allergens in the development of early allergic sensitization and asthmatic airways disorders.***

<u>Descriptive statistics:</u> Study participants will be characterized with regard to demographic variables such as age, gender, and race; clinical variables such as symptom/medication use frequency, healthcare utilization, allergy sensitivity and pulmonary function, and environmental variables such as indoor allergens (cockroach, mouse, cat, and dust mite). Categorical variables will be summarized by frequencies, while continuous variables will be summarized by mean, standard deviation, median, and range. Levels of mold, indoor allergens, pesticides, and VOCs will be log-transformed to compute geometric means and geometric standard deviations. Where appropriate, other transformations or non-parametric analysis methods will be used.

<u>Regression models:</u> In general, for the regression analyses, primary interest lies in the coefficients for the binary "exposure" variable (green vs. comparison). The regressions will also include background variables such as pesticide, VOC, and allergen levels; these variables are included to adjust for differences between households, and we are particularly interested in the coefficients. We will also include interactions between exposure and the background variables. Significant coefficients for these interactions are important because they imply that the exposure has a larger effect under some conditions in comparison to others. In addition, it will be important to consider nonlinear models to allow, for example, for a threshold of allergen exposure.

In the case of dichotomous outcomes, multiple logistic regression will be used to calculate odds ratios (in the case of rare events such as overnight hospitalizations due to asthma attacks). When rare events exceed 10%, then risk ratios will be calculated from the logistic regression (J. Zhang & Yu, 1998). Hierarchical linear modeling will be used for evaluating effects of individual apartment, neighborhood and regional factors on levels of environmental agents. The main

outcomes are allergen, VOC, and pesticide levels in the home; however, several factors should be adjusted in the analysis, including but not limited to smoking in the home, proximity to major roadways, and region of the country. For example, researchers in Baltimore found a low prevalence of both cockroach exposure and sensitization among children in high SES African American families (Sarpong, Hamilton, Eggleston, & Adkinson, 1996). This observation highlights a possible mechanism through which factors operating at the social/environmental level (e.g., deteriorated built environment) might contribute to asthma among disadvantaged urban children, i.e., via increased exposure to indoor allergens (Rauh et al., 2002). Conceivably, the greenest of homes could still have poor indoor air quality due to some of the aforementioned factors.

The analytical plan for specific hypotheses are:

Hypothesis 1: Green housing will lead to 1) lower levels of environmental contaminants compared with those of comparison housing, and 2) lower levels of related biomarkers in the residents of green vs. comparison housing. (Note: Hypotheses are abbreviated here for brevity. For complete wording of hypotheses see Part A)

The longitudinal study here outlined will permit estimation of:

- Geometric mean (GM) and standard deviation (GSD) for each of the environmental analytes (e.g., pesticides, VOCs, mold, and indoor allergens) by rehabilitation type (green vs. comparison).
- Geometric mean (GM) and standard deviation (GSD) for each of the biomarkers for pesticides and VOCs by rehabilitation type (green vs. comparison).
- Correlations between environmental measurements and biomarkers (stratified by several characteristics including but not limited to age and gender).
- Proportion of green vs. comparison homes that have pesticides that are currently banned for residential use by EPA.

If irritants and allergens are lower in green vs. comparison housing, children with asthma (ages 7-12) living in green housing should experience fewer and less severe asthma exacerbations. (Note: Hypothesis is abbreviated here for brevity. For complete wording of hypothesis see Part A)

The longitudinal study here outlined will permit estimation of:

Odds ratios (OR) or Rate Ratios (RR) for exposures to environmental agents and cumulative incidence of wheeze and/or other asthma-related morbidity measurements (among children ages 7-12 with asthma).

Missing data: We anticipate the inevitable occurrence of missing data, including dropouts. First, if the missingness of the data is sufficiently small and the associations of interest are sufficiently large, the simple device of imputing upper and lower bound data, if possible, will suffice. That is, a small amount of missing data and a large effect size will allow a unique inference to stand no matter whether the missing data are imputed at their minimum or maximum possible values and used as such. This is consistent with the most conservative approaches adopted in clinical

trials wherein subjects lost to follow-up are assumed to have died or to have otherwise suffered the worst possible endpoint. In general however, we must anticipate that we may be facing larger missingness and/or smaller effect sizes and/or impractical upper and lower bounds, such that primary inference changes between the extremes. In this case we will use the multiple imputation procedure of Rubin (Rubin, 1985) to address the problem. In this technique, a fair amount of effort is devoted to the construction of an imputation model or set of models to provide best estimates of missing endpoints. These best estimates may include the best case or worst case scenarios; the point is that they should most fairly represent data that are missing given the observable information at hand. The imputation models may need to assume data missing at random or they may need further specification to allow for non-ignorable missingness. Each analysis be developed using the best imputation model for missing data for that analysis, using available observed covariates and non-missing endpoints.

## B.3. METHODS TO MAXIMIZE RESPONSE RATES AND DEAL WITH NONRESPONSE

Two large-scale housing intervention studies in low-income neighborhoods that had a 1-year follow-up have reported response rates of 92-93% (Morgan et al., 2004; Persky et al., 2009). We anticipate that once enrolled into the Green Housing study, participants will have at least an 80% response rate for completion of the 1-yr study.

We have two strategies to maximize response rates of the enrolled participants: 1) Study participants (mothers/ primary caregivers of children enrolled in study) will receive compensation for their participation as they complete the required study activities throughout the 1-year duration. (See section A.9 INCENTIVES FOR RESPONDENTS for details) and 2) We will also give study results to the participants. Other investigators have found that study participants often wish to know their results (Brody et al., 2007). By offering an in-person discussion of their results during their last home visit, we hope to maximize the chance for completion of their 1-yr follow-up. If we experience a loss-to-follow-up greater than 80%, our contingency plan is to meet with HUD partners to possibly add another study site.

We have the following instructions for trying to contact difficult-to-reach participants: 1) At least 10 attempts will be made and documented in an effort to reach the participant; 2) Calls and visits to the participants will be made at various times of days (mainly between 10am- 8pm) and on different days of the week at a time convenient to the study participant; 3) When leaving a message, the trained technician will leave his/her name, the name of his/her institution, the reason for the call (i.e., housing study, and the call-back number; and 4) The technician will try calling “alternate contacts” to reach the study participants.

## B.4. TESTS OF PROCEDURES OR METHODS TO BE UNDERTAKEN

The Green Housing Study questionnaires were primarily based on questions from national health and housing surveys and different epidemiologic studies (e.g., The Inner-City Asthma Study, ICAS) that were conducted in different parts of the country among similar low-income, inner city children with asthma. The national surveys include the following:

The National Children’s Study (NCS)

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The National Health and Nutrition Examination Survey (NHANES)
The National Health Interview Survey (NHIS)
The Behavioral Risk Factor Surveillance System (BRFSS)
The Current Population Survey (CPS)
The American Healthy Homes Survey (AHHS)
The American Housing Survey (AHS)

Results from the research studies have been extensively published in peer-reviewed environmental health journals that provided scientific basis for home-based asthma intervention studies (Wilson et al., 2009). Some questions from these studies were included verbatim in the Green Housing Study baseline questionnaire, some were modified to fit our study framework, and some additional questions were added (Table 24). CDC epidemiologists modified some of the existing questions and developed new questions in consultation with academic peers and subject matter experts.

Table 24. Examples of questions used in the Green Housing Study and their provenance.

| Questions | Questionnaire Type | Question | Name of the study | Reference article |
|---|---|---|---|---|
| Included verbatim | Baseline (Home characteristics) | In the last 3 days: today or yesterday or the day before yesterday, have you either breathed fumes from **gasoline** or had it on your skin? | NHANES | n/a |
| | Baseline (Child with asthma age 7-12) | Is [Child's name] currently covered by any kind of health insurance or some other health care plan? | NCS | n/a |
| | Illness checklist | Did you receive Tamiflu® or oseltamivir [*o sel TAM i veer*] or an inhaled medicine called Relenza® or zanamivir [*za NA mi veer*] to treat this illness? | BRFSS | n/a |
| Included with minor modifications | 6 and 12 month follow-up (Child with asthma age 7-12)<br>* note: the mother or primary caregiver answers this question, not the child. | Green Housing Study version: In the last 3 months, did [Child's name] receive Tamiflu® or oseltamivir [*o sel TAM i veer*] or an inhaled medicine called Relenza® or zanamivir [*za NA mi veer*] to treat this illness?<br>BRFSS version: Last month, did you receive Tamiflu® or oseltamivir [*o sel TAM i veer*] or an inhaled medicine called Relenza® or zanamivir [*za NA mi veer*] to treat this illness? | BRFSS<br><br>And also recent H1N1 flu pandemic surveillance | Cauchemez S, Donnelly CA, Reed C, Ghani AC, Fraser C, Kent CK, Finelli L, Ferguson NM. Household transmission of 2009 pandemic influenza A (H1N1) virus in the United States. N Engl J Med. 2009 Dec 31;361(27):2619-27. |

After development of initial draft, the baseline questionnaire was distributed among CDC, NIH, EPA, and HUD colleagues and five non-federal academic peers (Drs. Gary Adamkiewicz, Brett Singer, Mark Mendell, Doug Brugge, and Tiina Reponen) for face and content validation. Based on repeated feedback received from peers, the questionnaire underwent multiple revisions before a final draft was prepared. Cognitive interviews with nine or fewer college-educated CDC colleagues were conducted in a controlled environment. The questionnaire underwent a final revision based on the responses from participants. Some of the results from this pilot testing are shown below.

Each of the questionnaires was pilot-tested at CDC on nine or fewer (in some cases not all 9 were available to participate) predominantly college-educated CDC employee-volunteers during non-work hours. The pilot tests were administered by two Green Housing Study researchers. The results of our pilot testing are shown in Table 25. Based upon pilot testing, the questionnaires were revised to increase ease of understanding and speed of response. We conservatively estimated the response times for our study participants (low-income mothers/primary caregivers living in multifamily, urban housing) based on the average response times recorded during our pilot tests.

Table 25. Pilot test of each questionnaire and estimated response time for study participants

| Form name | Average response time (minutes) | Minimum response time (minutes) | Maximum response time (minutes) | Estimated response time for study participants |
|---|---|---|---|---|
| Screening questionnaire | 4:52 | 2:16 | 7:57 | 10 |
| Baseline Questionnaire (Home Characteristics) | 6:03 | 4:37 | 7:15 | 15 |
| Baseline Questionnaire (Part 2: Home Characteristics) | 2:56 | 2:26 | 3:31 | 5 |
| Baseline Questionnaire (Mother/primary caregiver) | 0:58 | 0:50 | 1:15 | 5 |
| Baseline Questionnaire (for Children with asthma 7-12 years) | 6:38 | 6:20 | 6:50 | 15 |
| 3 and 9-month Phone contact | 2:30 | 2:15 | 2:45 | 5 |
| 6 and 12-month Follow-up Questionnaire (for environment) | 3:52 | 3:10 | 4:20 | 10 |
| 6 and 12-month Follow-up Questionnaire (for children with asthma 7-12) | 3:07 | 3:00 | 3:15 | 10 |
| Time/Activity form (for Mothers/primary caregivers of enrolled children) | 1:45 | 1:40 | 2:00 | 5 |
| Time/Activity form (for Children with asthma 7-12 yrs) | 0:40 | 0:35 | 0:50 | 5 |
| Illness Checklist | 1:05 | 0:45 | 1:25 | 5 |

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

**Appendix C (The IRB-approved Protocol)**

*Individuals Consulted on Statistical Aspects of the Design*

| | | |
|---|---|---|
| Curtis Blanton, MS | CDC/NCEH | (770) 488-7114 |
| Dana Flanders, Ph.D. | CDC/NCEH | (770) 488-3472 |
| Rey DeCastro, ScD. | CDC/NCEH | (770) 488-0162 |
| Carol Gotway Crawford, Ph.D. | CDC/OD | (404) 498-6023 |
| Andrew Gelman, Ph.D. | Columbia University | (212) 851-2142 |

***GRANTEE RESPONSIBLE FOR COLLECTING INFORMATION FOR THE AGENCY***

**GRANTEE NAME: TBD**

**GRANTEE ADDRESS: TBD**

***GRANTEE RESPONSIBLE FOR ANALYZING INFORMATION FOR THE AGENCY***

**NOT APPLICABLE. CDC WILL ANALYZE DATA.**

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# APPENDIX B

Table B-1 lists additional chemicals and media. Should resources allow, media will be analyzed for additional chemicals as shown in the table.

**Appendix C (The IRB-approved Protocol)**

Table B-1. Additional chemical and biological agents to be considered if resources allow for the EPA pilot study add-on.

| Target Compound Class | Target Chemical/Biological | | Media | Biomarkers |
|---|---|---|---|---|
| **Consumer Product Active Ingredients** | | 2-Butoxyethanol | Indoor air, dust, surface wipe, hand wipe, duplicate diet, urine, blood, soil | 2-butoxyacetic acid (and conjugate) |
| | | Linalool | Soil, hand wipe, blood | -[a] |
| | | Limonene | Soil, hand wipe, blood | -[a] |
| | | Pinene | Indoor air, dust, surface wipe, hand wipe, duplicate diet, urine, blood, soil | -[a] |
| | | Diethanolamine | Indoor air, dust, surface wipe, hand wipe, duplicate diet, urine, blood, soil | -[a] |
| | | Monoethanolamine | Indoor air, dust, surface wipe, hand wipe, duplicate diet, urine, blood, soil | -[a] |
| | | Methyl paraben | Soil, hand wipe, blood | Methyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | | Propyl paraben | Soil, hand wipe, blood | Propyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | | Butyl paraben | Soil, hand wipe, blood | Butyl paraben conjugates, *p*-hydroxybenzoic acid and conjugates |
| | | Methoxypropanol | Indoor air, dust, surface wipe, hand wipe, duplicate diet, urine, blood, soil | -[a] |
| | | Triclosan | Indoor air, hand wipe, duplicate diet, blood, urine, soil | Triclosan conjugates, 2,4-dichlorophenol (2,4-DCP) |
| **BPA and Replacement Chemicals** | | BPA | All media[b] | BPA glucuronide, sulfate conjugates |
| | | BPS | All media[b] | -[a] |
| | | BPP | All media[b] | -[a] |
| | | BPF | All media[b] | -[a] |
| | | BPB | All media[b] | -[a] |
| | | BPZ | All media[b] | -[a] |
| **Flame Retardants** | PBDEs | BDE47 | All media[b] | -[a] |
| | | BDE99 | All media[b] | -[a] |
| | | BDE100 | All media[b] | -[a] |
| | | BDE153 | All media[b] | -[a] |
| | OPs | TCPP | All media[b] | -[a] |

| | | | | |
|---|---|---|---|---|
| | | TCEP | All media[b] | -[a] |
| | | TDCPP | All media[b] | -[a] |
| | | TPP | All media[b] | -[a] |
| | OCs | Chlordane | All media[b] | Oxychlordane |
| | | DDT | All media[b] | DDD, DDE |
| | | Endosulfan | All media[b] | Endosulfan sulfate, endosulfan ether, endosulfan lactone |
| | | Pentachlorophenol | All media[b] | TCHQ |
| | OPs | Acephate | All media[b] | -[a] |
| | | Dichlorvos (DDVP) | All media[b] | Dichloroacetaldehyde, dichloroacetic acid |
| | | Malathion | All media[b] | Malaoxon DCA, malathion MCA, o,o-DMPT, DEDTP, o,o-DMDTP, o,o-DMP, 2-[(dimethoxyphosphorothioyl) sulfanyl] succinic acid (malathion dicarboxylic acid) |
| | | TCVP (Tetrachlorovinphos) | All media[b] | DMP |
| | | Trichlorfon | All media[b] | Dichlorvos |
| | Pyrethroids | Allethrin | All media[b] | -[a] |
| | | Bifenthrin | All media[b] | 2-methyl-3-phenylbenzoic acid (MPA) |
| | | Cyfluthrin | All media[b] | 4F-3PBA, *cis/trans*-DCCA |
| | | *Lambda*-Cyhalothrin | All media[b] | 3-PBA, 3-PBA glucuronide/glycine conjugates |
| **Pesticides** | | Cypermethrin | All media[b] | 3-PBA, 3-PBA glucuronide/glycine conjugates, *cis/trans*-DCCA |
| | | Cyphenothrin | All media[b] | 3-PBA, 3-PBA glucuronide/glycine conjugates |
| | | Deltamethrin | All media[b] | 4'-OH deltamethrin, *cis/ trans*-DBCA, *cis/trans*-DBCA glycine, *cis/trans*-DBCA glucuronide |
| | | Esfenvalerate | All media[b] | 3-PBA, 3-PBA glucuronide/glycine conjugates |
| | | Imiprothrin | All media[b] | -[a] |
| | | Metofluthrin | All media[b] | HOCH2-FB-Al, MCA, CH3OCH2-FB-Al |
| | | Prallethrin | All media[b] | -[a] |
| | | Pyrethrins | All media[b] | *trans*-chrysanthemum dicarboxylic acid (CDCA) |

| | | | | |
|---|---|---|---|---|
| | Carbamates | Resmethrin | All media[b] | -[a] |
| | | Tetramethrin | All media[b] | -[a] |
| | | Tralomethrin | All media[b] | -[a] |
| | | Aldicarb | All media[b] | Aldicarb sulfoxide |
| | | Carbaryl | All media[b] | 1-naphthol + sulfate /glucuronide conjugates, 4-(Hydroxy)-1-naphthyl N-methyl carbamate + glucuronide conjugate |
| | | Propoxur | All media[b] | -[a] |
| | Juvenile Hormone Analog | Pyriproxyfen | All media[b] | -[a] |
| | Pediculicide | Spinosad | All media[b] | -[a] |
| | Trifluoromethyl aminohydrazone | Hydramethylnon | All media[b] | -[a] |
| | Herbicides | 2,4-D | All media[b] | 2,4-dichlorophenol (2,4-DCP) |
| | | Atrazine | All media[b] | -[a] |
| | | Bensulide | All media[b] | -[a] |
| | | Dicamba | All media[b] | -[a] |
| | | Glyphosate Amine | All media[b] | -[a] |
| | Amidine insecticide | Amitraz | All media[b] | -[a] |
| | Neonicitinoids | Imidacloprid | All media[b] | 6-chloronicotinic acid |
| | | Thiamethoxam | All media[b] | -[a] |
| | Insect Growth Regulators | Azadirachtin | All media[b] | -[a] |
| | | Novaluron | All media[b] | -[a] |
| **Perfluorinated Compounds** | | C4 – C14 carboxylic acids | Dust, soil, hand wipe, blood | -[a] |
| | | PFOS | Dust, soil, hand wipe, blood | -[a] |
| | | PFBS | Dust, soil, hand wipe, blood | -[a] |
| | | PFHS | Dust, soil, hand wipe, blood | -[a] |
| | | PFDS | Dust, soil, hand wipe, blood | -[a] |
| **Metals** | | Aluminum | Socks | -[a] |
| | | Arsenic | Socks | -[a] |
| | | Cadmium | Socks | -[a] |
| | | Silicon | Socks | -[a] |
| | | Titanium | Socks | -[a] |
| **General Biomarkers** | | | | acetylcholinesterase (AChE), butyrylcholinesterase, leukotrienes, cortisol, cytokines, creatinine |
| **Untargeted analyses** | | | Dust, duplicate diet, urine | |

[a]Denotes biomarker is parent compound.

[b]See Table 4 for a complete list of media.

# APPENDIX C

Location, Transportation, Activity, Diet, Consumer Products, and Home Observation Questionnaire (CDC IRB Approved, IRB#5587, April 2013)

## Appendix C (The IRB-approved Protocol)

Household ID#

Child's Age

Child's Gender

- F
- M

Date

Interviewer's Initials

**A. Introductory Questions (To be completed by field technician and participant)**

1. Has your child been diagnosed with asthma by a doctor?

- Yes
- No
- Don't Know/Refused to answer

2. Did your child experience any asthma symptoms yesterday (e.g., wheezing, shortness of breath, tightness in chest, dry cough)?

- Yes
- No
- Don't Know/Refused to answer

## Appendix C (The IRB-approved Protocol)

### B. Location Questions (To be completed by field technician and participant)

3. For each approximate time period given below, indicate where your child was located. Select any locations that apply to the time period.

| | Home | Outdoor area at home | Other residence (ex. babysitter's house) | Store | Restaurant | Church | Other indoor location | Park | Bus/train stop | On or near street | Parking garage | Other outdoor location | In vehicle | Don't know/Refused to answer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5:00 am - 5:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:30 am - 5:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:00 am - 6:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:30 am - 6:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:00 am - 7:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:30 am - 7:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:00 am - 8:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:30 am - 8:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:00 am - 9:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:30 am - 9:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## Appendix C (The IRB-approved Protocol)

| | Home | Outdoor area at home | Other residence (ex. babysitter's house) | Store | Restaurant | Church | Other indoor location | Park | Bus/train stop | On or near street | Parking garage | Other outdoor location | In vehicle | Don't know/Refused to answer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10:00 am - 10:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10:30 am - 10:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:00 am - 11:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:30 am - 11:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12:00 pm - 12:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12:30 pm - 12:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 1:00 pm - 1:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 1:30 pm - 1:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2:00 pm - 2:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2:30 pm - 2:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3:00 pm - 3:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## Appendix C (The IRB-approved Protocol)

| | Home | Outdoor area at home | Other residence (ex. babysitter's house) | Store | Restaurant | Church | Other indoor location | Park | Bus/train stop | On or near street | Parking garage | Other outdoor location | In vehicle | Don't know/Refused to answer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3:30 pm - 3:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4:00 pm - 4:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4:30 pm - 4:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:00 pm - 5:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:30 pm - 5:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:00 pm - 6:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:30 pm - 6:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:00 pm - 7:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:30 pm - 7:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:00 pm - 8:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:30 pm - 8:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## Appendix C (The IRB-approved Protocol)

| | Home | Outdoor area at home | Other residence (ex. babysitter's house) | Store | Restaurant | Church | Other indoor location | Park | Bus/train stop | On or near street | Parking garage | Other outdoor location | In vehicle | Don't know/Refused to answer |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 9:00 pm - 9:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:30 pm - 9:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10:00 pm - 10:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10:30 pm - 10:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:00 pm - 11:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:30 pm - 11:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

4. Look back at the answers to question 3. Based on yesterday's day of the week, do these locations represent a fairly typical or normal day for your child? For example, if yesterday was a weekday, is this a typical weekday schedule for your child?

- ○ Yes
- ○ No
- ○ Don't know/Refused to answer

## Appendix C (The IRB-approved Protocol)

### C. Activity Questions (To be completed by field technician and participant)

5. For each approximate time period given below, indicate activities your child performed. Select all that apply for the time period.

| | Dress, groom or bathe | Eat | Watch TV | Play | Use computer or play video games | Read or do school work | Take care of younger children | Chores | Exercise | Play with pet | Arts and crafts | Sleep | Don't know/Refused to answer | None of these |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5:00 am - 5:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:30 am - 5:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:00 am - 6:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:30 am - 6:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:00 am - 7:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:30 am - 7:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:00 am - 8:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:30 am - 8:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:00 am - 9:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:30 am - 9:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

| | Dress, groom or bathe | Eat | Watch TV | Play | Use computer or play video games | Read or do school work | Take care of younger children | Chores | Exercise | Play with pet | Arts and crafts | Sleep | Don't know/Refused to answer | None of these |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10:00 am - 10:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10:30 am - 10:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:00 am - 11:29 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:30 am - 11:59 am | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12:00 pm - 12:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12:30 pm - 12:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 1:00 pm - 1:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 1:30 pm - 1:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2:00 pm - 2:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 2:30 pm - 2:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3:00 pm - 3:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3:30 pm - 3:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## Appendix C (The IRB-approved Protocol)

| | Dress, groom or bathe | Eat | Watch TV | Play | Use computer or play video games | Read or do school work | Take care of younger children | Chores | Exercise | Play with pet | Arts and crafts | Sleep | Don't know/Refused to answer | None of these |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4:00 pm - 4:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4:30 pm - 4:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:00 pm - 5:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 5:30 pm - 5:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:00 pm - 6:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 6:30 pm - 6:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:00 pm - 7:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 7:30 pm - 7:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:00 pm - 8:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 8:30 pm - 8:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:00 pm - 9:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 9:30 pm - 9:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

## Appendix C (The IRB-approved Protocol)

| | Dress, groom or bathe | Eat | Watch TV | Play | Use computer or play video games | Read or do school work | Take care of younger children | Chores | Exercise | Play with pet | Arts and crafts | Sleep | Don't know/Refused to answer | None of these |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10:00 pm - 10:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10:30 pm - 10:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:00 pm - 11:29 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 11:30 pm - 11:59 pm | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

6. When at home, which room does your child sleep in?
- ○ Child's bedroom
- ○ Mother's bedroom
- ○ Living room
- ○ Other room in the home
- ○ Don't know/Refused to answer

7. When indoors at home and awake, where does your child spend the most time?
- ○ Living room/family room
- ○ Child's bedroom
- ○ Mother's bedroom
- ○ Kitchen
- ○ Other room in the home
- ○ Don't know/Refused to answer

8. When at home, how much time per day does your child spend sitting/playing/lying on the floor?
- ○ Less than 30 minutes
- ○ 30 minutes
- ○ 1 hr
- ○ 1.5 hrs
- ○ 2 hrs
- ○ 2.5 hrs
- ○ 3 hrs
- ○ More than 3 hrs
- ○ Don't know/Refused to answer

9. Is the floor she or he plays on carpeted?
- ○ Carpeted
- ○ Not carpeted
- ○ Partially carpeted
- ○ Child does not play/sit/lie on the floor
- ○ Don't know/Refused to answer

10. Typically, how much time per day does your child play outside at home (yard, common area, playground)?

- ○ 0-15 minutes
- ○ 15-30 minutes
- ○ 30 minutes to 1 hour
- ○ 1-2 hours
- ○ 2-3 hours
- ○ More than 3 hours
- ○ Don’t know/Refused to answer

11. Typically, how much time per day does your child play outside at school/daycare?

- ○ 0-15 minutes
- ○ 15-30 minutes
- ○ 30 minutes to 1 hour
- ○ 1-2 hours
- ○ 2-3 hours
- ○ More than 3 hours
- ○ Don’t know/Refused to answer

12. How much time per day does your child play at local parks?

- ○ 0-15 minutes
- ○ 15-30 minutes
- ○ 30 minutes to 1 hour
- ○ 1-2 hours
- ○ 2-3 hours
- ○ More than 3 hours
- ○ Don’t know/Refused to answer

13. How often does your child's sleep get interrupted (e.g., by noise or other disturbance in the community)?

- ○ Never
- ○ Once a month
- ○ Once a week
- ○ More than once a week
- ○ Don't know/Refused to answer

14. How many times did your child wash his/her hands yesterday?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ More than 7
- ○ Don't know/Refused to answer

15. How many times a week does your child bathe?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ More than 7
- ○ Don't know/Refused to answer

**D. Diet Questions (To be completed by field technician and participant)**

16. How many meals did your child eat yesterday (e.g., breakfast, lunch, dinner), not counting snacks?

- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ More than 7
- ○ Don't know/Refused to answer

17. For each MEAL your child ate, what best describes the meal? If your child ate more than 4 meals, just answer for the first 4.

| | Meal prepared by school | Meal made at home from ready-made frozen or canned food | Fast food meal | Restaurant meal (not fast food) | Meal made at home from scratch | Don't know/Refused to answer |
|---|---|---|---|---|---|---|
| Meal 1 | ○ | ○ | ○ | ○ | ○ | ○ |
| Meal 2 | ○ | ○ | ○ | ○ | ○ | ○ |
| Meal 3 | ○ | ○ | ○ | ○ | ○ | ○ |
| Meal 4 | ○ | ○ | ○ | ○ | ○ | ○ |

18. On average, how often does your child eat/drink the following foods and beverages?

| | Once a month or less | 2-3 times per month | 1-2 times per week | 3-4 times per week | 5-6 times per week | Once a day | 2-3 times per day | 4-5 times per day | 6 or more times per day |
|---|---|---|---|---|---|---|---|---|---|
| Poultry | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Beef | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Pork | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Fish | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Shellfish | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Rice | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Other dairy products (not milk) | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Leafy green vegetables | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Other vegetables (not potatoes) | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Potatoes | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Breads | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Fruit | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Snack Foods | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Milk | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Fruit juice | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Soda | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Tap water or beverage made with tap water | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

19. How often do you purchase food at each of these types of stores?

| | Never | Once a month | Once a week | 2 times a week | 3 times a week | More than 3 times a week |
|---|---|---|---|---|---|---|
| Supermarket or large grocery store | ○ | ○ | ○ | ○ | ○ | ○ |
| Small grocery store (e.g., small store in your neighborhood that mainly sells food) | ○ | ○ | ○ | ○ | ○ | ○ |
| Farmer's or outdoor market | ○ | ○ | ○ | ○ | ○ | ○ |
| Store in a gas station | ○ | ○ | ○ | ○ | ○ | ○ |
| Discount store (e.g., a dollar store, Big Lots) | ○ | ○ | ○ | ○ | ○ | ○ |

20. How often does your child eat at each of these types of restaurants?

| | Never | Once a month | Once a week | 2 times a week | 3 times a week | More than 3 times a week |
|---|---|---|---|---|---|---|
| Fast food | ○ | ○ | ○ | ○ | ○ | ○ |
| Sit - down restaurant | ○ | ○ | ○ | ○ | ○ | ○ |
| Food truck or stand | ○ | ○ | ○ | ○ | ○ | ○ |

**E. Household Cleaning Products (To be completed by field technician and participant)**

21. Please select use frequency for each product type inside your home

| | Daily | Weekly | Monthly | Yearly/ Never |
|---|---|---|---|---|
| All-purpose cleaner | ○ | ○ | ○ | ○ |
| Glass cleaner | ○ | ○ | ○ | ○ |
| Floor cleaner | ○ | ○ | ○ | ○ |
| Toilet bowl cleaner | ○ | ○ | ○ | ○ |
| Carpet cleaner | ○ | ○ | ○ | ○ |
| Polish or wax | ○ | ○ | ○ | ○ |
| Air freshener | ○ | ○ | ○ | ○ |
| Disinfectant Spray | ○ | ○ | ○ | ○ |
| Laundry detergent | ○ | ○ | ○ | ○ |
| Dryer sheets | ○ | ○ | ○ | ○ |
| Stain/spot remover | ○ | ○ | ○ | ○ |

**F. Personal Care Products (To be completed by field technician and participant)**

22. Please select use frequency for each product type inside your home

| | Daily | Weekly | Monthly | Yearly/ Never |
|---|---|---|---|---|
| Shampoo | ○ | ○ | ○ | ○ |
| Liquid hand soap | ○ | ○ | ○ | ○ |
| Hand sanitizer | ○ | ○ | ○ | ○ |
| Hand/body lotion | ○ | ○ | ○ | ○ |
| Facial moisturizer | ○ | ○ | ○ | ○ |
| Fragrance/perfume | ○ | ○ | ○ | ○ |
| Hair styling products | ○ | ○ | ○ | ○ |
| Sunscreen | ○ | ○ | ○ | ○ |

**G. Consumer Product Classes (To be completed by field technician and participant)**

23. Please select use frequency for each product type inside/near your home

| | Daily | Weekly | Monthly | Yearly/ Never |
|---|---|---|---|---|
| Arts and Crafts Products | ○ | ○ | ○ | ○ |
| Automotive Products | ○ | ○ | ○ | ○ |
| Home Maintenance | ○ | ○ | ○ | ○ |
| Cleaning Products | ○ | ○ | ○ | ○ |
| Personal Care Products | ○ | ○ | ○ | ○ |
| Pesticides | ○ | ○ | ○ | ○ |
| Pet Care Products | ○ | ○ | ○ | ○ |
| Home Office | ○ | ○ | ○ | ○ |
| Landscape and Yard | ○ | ○ | ○ | ○ |

**H. Home Observations (To be completed by field technician with input from participant as needed)**

24a. Select the answer(s) that best describe the percentage of total floor area in the home.

| | 0 | 1-20 | 21-40 | 41-60 | 61-80 | 81-100 |
|---|---|---|---|---|---|---|
| % Covered by carpet or rug | ○ | ○ | ○ | ○ | ○ | ○ |
| % Exposed linoleum or linoleum tile | ○ | ○ | ○ | ○ | ○ | ○ |
| % Exposed wood or wood laminate | ○ | ○ | ○ | ○ | ○ | ○ |
| % Exposed ceramic or stone tile | ○ | ○ | ○ | ○ | ○ | ○ |
| % Exposed other | ○ | ○ | ○ | ○ | ○ | ○ |

24b. If a percentage of the floor was "Other," what was the material?

25a. Select the answer(s) that best describe the home's furniture.

| | 0 | 1 | 2 | 3 | 4 | 5 or more |
|---|---|---|---|---|---|---|
| Number of upholstered sofas | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of upholstered chairs | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of other upholstered furniture | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of twin beds w mattresses | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of double beds w mattresses | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of queen beds w mattresses | ○ | ○ | ○ | ○ | ○ | ○ |
| Number of king beds w mattresses | ○ | ○ | ○ | ○ | ○ | ○ |

25b. Select the answer(s) that best describe the percentage of upholstery material for the home's furniture.

| | 0 | 1-20 | 21-40 | 41-60 | 61-80 | 81-100 |
|---|---|---|---|---|---|---|
| % Fabric covering | ○ | ○ | ○ | ○ | ○ | ○ |
| % Vinyl covering | ○ | ○ | ○ | ○ | ○ | ○ |
| % Leather covering | ○ | ○ | ○ | ○ | ○ | ○ |
| % Other | ○ | ○ | ○ | ○ | ○ | ○ |

**I. Indoor Cleanliness (To be completed by field technician)**

**Whole House Rating for Indoor Residential Cleanliness**

26. Select one cleanliness rating for each category, where 1 is low (most clean) and 5 is high (least clean). These ratings apply to the whole house. To be completed by technician observation.

| | 1 (Low) | 2 | 3 | 4 | 5 (High) |
|---|---|---|---|---|---|
| Clutter on floor, tables, counters, furniture | ○ | ○ | ○ | ○ | ○ |
| Extent and thickness of dust on surfaces | ○ | ○ | ○ | ○ | ○ |
| Dirt/mold on floor, walls, ceiling | ○ | ○ | ○ | ○ | ○ |
| Peeling interior paint | ○ | ○ | ○ | ○ | ○ |
| Visible pet hair on floor and furniture | ○ | ○ | ○ | ○ | ○ |
| Visible food/crumbs on counters and tables | ○ | ○ | ○ | ○ | ○ |
| Insect/Rodent problem | ○ | ○ | ○ | ○ | ○ |

27. Select one overall rating of cleanliness for the home. Select a value from a range of 1, Cleanest, to 5, Least Clean.

| | 1 | 2 | 3 | 4 | 5 | |
|---|---|---|---|---|---|---|
| Cleanest | ○ | ○ | ○ | ○ | ○ | Least Clean |

## J. Outdoor Housing Information (To be completed by field technician)

28. Residence door is on floor

- ○ Below ground
- ○ Ground
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ 8
- ○ 9
- ○ >=10

29. Primary residence door opens to

- ○ Interior Hallway
- ○ Exterior Walkway
- ○ Individual or duplex porch
- ○ Individual or duplex stoop
- ○ Other: _____

30. Is there a designated playground or play area (not including basketball courts)?

- ○ Yes
- ○ No

31a. If there is a designated playground or play area, what is the composition of its surface?

| | 0 | 1-20 | 21-40 | 41-60 | 61-80 | 81-100 |
|---|---|---|---|---|---|---|
| Grass | ○ | ○ | ○ | ○ | ○ | ○ |
| Bare soil | ○ | ○ | ○ | ○ | ○ | ○ |
| Natural mulch or bark | ○ | ○ | ○ | ○ | ○ | ○ |
| Crumb rubber mulch | ○ | ○ | ○ | ○ | ○ | ○ |
| Rubber mats | ○ | ○ | ○ | ○ | ○ | ○ |
| Concrete | ○ | ○ | ○ | ○ | ○ | ○ |
| Asphalt | ○ | ○ | ○ | ○ | ○ | ○ |
| Other | ○ | ○ | ○ | ○ | ○ | ○ |

31b. If "Other" was selected above, please describe the surface.

# APPENDIX D

Considerations for Protection of Human Subjects in the Study

## Appendix C (The IRB-approved Protocol)

The U.S. EPA is dedicated to the utmost protection of human subjects who participate in their observational human exposure studies. To ensure the protection of human subjects, the EPA's National Exposure Research Laboratory (NERL) has developed state of the science information to help research scientists address specific elements when developing and implementing their observational human exposure studies. The *Scientific and Ethical Approaches for Observational Exposure Studies* (SEAOES) document developed by NERL (EPA 600/R-08/062, U.S. EPA, National Exposure Research Laboratory, Research Triangle Park, NC, 2008) provides information on regulatory requirements and ethical issues to consider when performing human subjects research. EPA researchers use the information and guidance in the SEAOES document and the *Guidance for Human Subjects Research in the National Exposure Research Laboratory* (EPA 600/R-10/175, U.S. EPA, National Exposure Research Laboratory, Research Triangle Park, NC, 2009) in the design of observational human exposure research studies. The following key elements in the SEAOES document are to be addressed when designing observational exposure research studies: study conceptualization and planning; ensuring protection of vulnerable groups; privacy, confidentiality, and other concerns related to observational human exposure studies; creating an appropriate relationship between the participant and researcher; building and maintaining appropriate community and stakeholder relationships; and designing and implementing strategies for effective communication. These key elements have been addressed by the EPA researchers in this research protocol.

As described in Section 7 of this research protocol, the study will be performed in accordance with human subject protections and procedures in place for the Green Housing Study. The protections and procedures have been developed and implemented at two prior study locations for the Green Housing Study at which the study has already been performed. The CDC Institutional Review Board (CDC IRB) has been responsible for human subject protections for the overall Green Housing Study and will be responsible for review of the human subjects research conducted under this EPA pilot study add-on to the Green Housing Study. The study protocol, consent and assent forms, and the questionnaire will be submitted for review and approval by the CDC IRB. Following CDC IRB approval, the protocol and IRB materials will be submitted to the U.S. EPA Human Subjects Research Review Official (HSRRO) for review and approval. No study recruitment or data collection shall proceed until the CDC IRB and EPA HSRRO approvals are obtained.

The following sections describe Considerations for the Protection of Human Subjects in this research protocol for the EPA pilot study add-on to the Green Housing Study. The considerations address key elements described in the SEAOES document. The elements described below generally follow the outline of the SEAOES document with the intent to highlight the human subject research considerations as related to the information and guidance in SEAOES. Preceding sections of this research protocol are referenced as appropriate.

**Appendix C (The IRB-approved Protocol)**

1.0 Elements to be considered in study conceptualization and planning

The research protocol for the EPA pilot study add-on to the Green Housing Study details the elements to be considered in study conceptualization and planning.

1.1 Justification for the Proposed Study

The mission of the U.S. Environmental Protection Agency (EPA) is to protect public health and safeguard the environment. The EPA Office of Research and Development's (ORD) Sustainable and Healthy Communities (SHC) Research Program is designed to help decision makers implement environmental management in ways that increase sustainable benefits, such as reducing or eliminating indoor exposures to pollutants from building materials, insecticides, or chemicals found in consumer products. Research conducted in the Enhancing Children's Health project in the SHC program (SHC project 2.2.2) develops the information and methods that decision makers need to assess how the natural and built environments affect children's health and well-being, such as asthma, obesity, and neurocognitive development.

Additionally, EPA ORD's Chemical Safety for Sustainability (CSS) Research Program is developing tools that will use systems approaches to advance the understanding of the links between exposures to chemicals and toxicity pathways that lead to the development of disease. More than 80,000 chemicals are currently listed or registered for use in the U.S. under EPA authorities and at least a thousand more are introduced every year. Many of these chemicals have not been thoroughly evaluated for their potential risks to human health, wildlife and the environment, particularly throughout their life cycle. As a result, a number of important aspects of chemical safety are not adequately understood, including the contribution of exposure to chemicals in the environment to the overall disease burden for susceptible populations. CSS research will dramatically increase the efficiency and speed of chemical evaluations, and will allow EPA to evaluate potential effects of chemical exposures on critical lifestages, such as the embryo and childhood, and other susceptibility factors, including genetics and co-existing diseases.

This EPA pilot study aims to support the needs of both ORD national research programs by addressing how young children's exposures to various indoor pollutants (both chemical and biological agents) change as a result of building renovation-based interventions, potentially affecting their asthma morbidity. This EPA pilot study is an add-on to the Green Housing Study. In addition to supporting EPA research programs, this pilot study will provide additional information on chemical exposures and children's interactions with their environments to enhance ongoing research in the Green Housing Study's evaluation of green housing and impacts on childhood asthma.

1.2 Justification for Including Human Subjects in the Research

EPA will leverage this opportunity to collect additional multimedia measurements and questionnaire data from the index children actively participating in the Green Housing Study and a sibling(s) in order to characterize personal, housing, and community factors influencing children's potential exposures to indoor contaminants at various lifestages. Additionally, by

recruiting sibling(s) of the index children, we will begin to examine how lifestage affects children's exposures when children have the potential to be exposed to the same chemicals in consumer products found in their environment. The objectives of this study can only be met by including human subjects (children and their caregivers) in the study because children's activities are key factors in their exposures to chemicals in their home environment.

1.3 Ensuring Scientific Validity of the Research Study

This research protocol describes the technical approach for the EPA pilot study add-on to the Green Housing Study third study site. It was developed by a team of researchers in the Office of Research and Development. This research protocol describes what data will be collected and how it will be analyzed to meet the study objectives. To ensure the scientific validity of the study, the research protocol will be subjected to an external peer review by experts in the field of exposure science and observational studies that involve human research subjects.

1.4 Ethical Issues in Ensuring Fair Subject Selection

CDC and its grantee will ensure fair subject selection for the Green Housing Study third study site through IRB-approved procedures.

1.5 Ensuring a Favorable Risk-Benefit Ratio

Benefits and risks of participation in the study have been considered by the CDC as part of the main Green Housing Study. Participation in the EPA pilot study add-on to the Green Housing Study does not change either the risks or the benefits to the participants.

1.6 Scientific and Ethical Reviews

This research protocol will be externally peer reviewed by three reviewers who are recognized experts in the field of exposure science and understand the complexities and sensitivities associated with conducting observational exposure measurement studies.

1.7 Conflicts of Interest

The EPA researchers are not aware of any conflicts of interest related this study, as discussed in the SEAOES document.

1.8 Considerations for Ensuring that Participant Behaviors are not Changed Adversely Because of Being in the Study

The SEAOES document discusses how changes in participant behavior may affect the study outcome. The Hawthorne Effect, for example, is well-recognized. The Green Housing Study is complicated because it involves building renovations while the participant is in the study (with pre- and post-renovation measurements). These renovations may be accompanied by changes in participant behavior. It would be difficult to determine if changes in participant behavior are due

to the renovations or participation in the observational study. No specific activities are planned to attempt to identify the latter.

1.9 Proposed Approaches for Monitoring Scientific and Ethical Issues During the Study

CDC and its grantee have IRB-approved approaches for monitoring scientific and ethical issues during the study.

2.0 Ensuring Protection of Vulnerable Groups

Concern for the protection of vulnerable groups is fundamental to modern ethical thought and guidelines. The Common Rule requires IRBs to assure that "additional safeguards have been included in the study to protect the rights and welfare of these [vulnerable] subjects". Researchers have to justify the involvement of vulnerable populations in the research study and include appropriate safeguards for protection of their safety and welfare. Children are identified as a vulnerable group.

2.1 Identification of Vulnerable Groups in the Study

The Common Rule identifies children as an example of a vulnerable group. EPA (40 CFR 26) and HHS (45 CFR 46) both extend additional protections to children when participating in observational exposure measurement studies. CDC and its grantee will ensure the protections of the children who participate in the Green Housing Study and the EPA pilot study add-on to the Green Housing Study through IRB-approved procedures.

2.2 Justification for Involving Vulnerable Persons in the Study

The main objective of the Green Housing Study is to understand how exposure levels change in green-renovated homes and how these changes affect asthma outcomes for children. This research is essential to improve children's health.

2.3 Consideration of Special Requirements for Vulnerable Groups (Children, Women, Other)

Children have long been recognized as a vulnerable group in research studies. EPA (40 CFR 26) and HHS (45 CFR 46) both extend additional protections to children when participating in observational exposure measurement studies. The participation of children in this observational human exposure study is critical to characterizing children's exposures to chemical and non-chemical stressors in their environment, which may exacerbate their asthma outcomes.

3.0 Privacy, Confidentiality, and Other Concerns Related to Observational Human Exposure Studies

Considerations for this element are described in the research protocol.

**Appendix C (The IRB-approved Protocol)**

3.1 Privacy Issues

Considerations for this element are described in the research protocol.

3.2 Confidentiality of Information and Participation

Considerations for this element are described in the research protocol.

3.3 Non-Study Hazards with Mandated Reporting Requirements

CDC and its grantee have procedures in place to identify, address, and report non-study hazards.

3.4 Other Non-Study Hazards

CDC and its grantee have procedures in place to identify, address, and report non-study hazards.

3.5 Third Party Issues

CDC and its grantee have procedures in place to address third party issues.

3.6 Plans for Data and Safety Monitoring and Oversight

CDC and its grantee have IRB-approved approaches for data and safety monitoring and oversight.

4.0 Creating an Appropriate Relationship between the Participant and Researcher

EPA researchers will not be involved in the selection of the study location, identification and recruitment of study participants, or interaction with study participants during the conduct of the study. The responsibility for this element is with CDC and its grantee.

4.1 Informed Consent Process

Considerations for this element are described in the research protocol.

4.2 Payments to Research Participants

No compensation will be provided to participants who participate in the EPA pilot study add-on to the Green Housing Study.

4.3 Research Rights and Grievance Procedures

CDC and its grantee have IRB-approved approaches for addressing research rights and grievance procedures.

4.4 Recruitment Strategies

EPA is not involved in participant recruitment. CDC and its grantee have IRB-approved approaches for recruitment.

4.5 Retention Strategies

EPA is not involved in participant retention. CDC and its grantee have IRB-approved approaches for retention of participants.

5.0 Building and Maintaining Appropriate Community and Stakeholder Relationships

EPA researchers will not be involved in the selection of the study location or working with community groups or stakeholders. CDC and its grantee will be responsible for this element.

6.0 Designing and Implementing Strategies for Effective Communication

EPA does not have a role in designing and implementing strategies for effective communication with the study participants, community groups, or other stakeholders. As part of the main Green Housing Study and its collaboration with HUD, this effort is the responsibility of CDC and its grantee.