Final Report: Literature Search on Housing and Neighborhood Characteristics and Conditions Related to Child Health and Development

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Work Assignment 7
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for

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1.0 BACKGROUND

The home environment and its surroundings have been shown to be important in determining the health and development of children. The purpose of this second interim report is to provide the National Children's Study (NCS) Program Office at NICHD background and information on the key housing and neighborhood factors that may be considered for measurement in the National Children's Study (NCS).

A literature review was conducted to gather background information and to broadly examine the existing body of knowledge on physical characteristics and conditions of housing and neighborhoods and their relationships to a specific set of children's health and developmental outcomes. The specific set of health outcomes investigated was based on an initial set of foundational, core hypotheses developed by the Interagency Coordinating Committee (ICC) for the NCS. The ICC proposed this set of core hypotheses to reflect the findings of 20 NCS working groups after independent reviews of the children's environmental health literature, and comments from a broad-based Study Assembly. The current list of NCS core hypotheses (as of November 2003) is included in Appendix A.

The first interim report under this Work Assignment presented an overview of initial results of the literature search. This overview included a preliminary summary of the quantity of literature found on housing and neighborhood risk factors associated with the NCS health and developmental outcomes, and a list of priority articles expected to be most useful in elucidating the relationship between a given housing/neighborhood risk factor and each relevant NCS hypotheses. For each of the five hypotheses, up to several hundred articles were initially identified through the literature search. Based on review of abstracts where available, approximately 230 of these articles were included in an initial list of potential priority articles. The initial list of articles, documented in the first interim report, was reviewed by the NCS Working Groups, and amended and revised as necessary based on work group input.

In this second interim report, the final list of articles approved by the NCS Working Groups is examined in detail. This examination does not represent a rigorous review or meta-analysis of the current research, but rather is intended to provide the NCS program office a broad picture of housing and neighborhood characteristics and conditions that have been reported in the literature to have associations with the health outcomes of interest to the NCS.

2.0 LITERATURE REVIEW METHODS

2.1 SCOPE AND LITERATURE SEARCH STRATEGY

The literature searches were conducted using the database vendor, DIALOG, an online web-based commercial service that provides a single user interface to over 800 literature source databases and allows simultaneous searching of multiple databases, combined with duplicate removal. Output can be formatted for input to a reference manager program such as ProCite.

To asses the relationship(s) between housing/neighborhood characteristics and child development/physical, mental, and neurological health, the following literature source databases were selected to provide a broad view of the hypotheses and incorporate the fields of health, the environment, toxicology, social sciences, and building engineering:

- MEDLINE (produced by the National library of Medicine)
- PsycInfo (American Psychological Association; online version of Psychological Abstracts)
- Ei Compendex (Elsevier Engineering; online version of Engineering Index)
- INSPEC (INSPEC/IEE)
- Wilson Social Science Abstracts (The HW Wilson Company)
- Enviroline (Congressional Information Service, Inc.)
- Social SciSearch (ISI/Institute for Scientific Information).

These bibliographic databases include literature from mainstream scientific and medical journals, including those focusing on pediatric health, sociology, anthropology, economics, psychology, environmental assessment, industrial hygiene, epidemiology, and preventive or community medicine, to ensure coverage of all major aspects of housing and neighborhood characteristics and conditions relevant to child health and development.

Keywords included in the literature search were extracted from, but not limited to, the five draft key hypotheses related to children's health and developmental outcomes. Additional keywords relating to housing or neighborhood factors in other areas of potential interest to the NCS, but not specifically called out in the key hypotheses (e.g., noise, persistent pesticides), were also included if known by Battelle or the Work Assignment Officer to be related either directly or indirectly to children's health or development from previous literature reviews conducted (e.g., those prepared by Battelle for the U.S. Department of Housing and Urban Development Healthy Homes Initiative).

Keywords used for the search are summarized in Table 2.1-1 below.

Table 2.1-1. Keywords Used in Literature Search, by Core Hypothesis

Overarching Keywords:
home, house, housing, residential, housing characteristics, housing deterioration
neighborhood, community, neighborhood characteristics, built environment
child, children, human health
Hypothesis 1: Pregnancy outcomes
pregnancy, stress, maternal stress, crime/violent crime/crime rates, infectious agents, infection, prenatal infection, perinatal infection, preterm birth, low birth weight, birth defects
Hypothesis 2: Neurodevelopment and behavior
pesticides, chlorpyrifos, diazinon, malathion, chlordane, mirex, DDT, carbaryl, human health, children's exposure, postnatal exposure, developmental disabilities, cognitive disabilities, intelligence quotient, IQ, psychiatric outcomes, schizophrenia, autism
Hypothesis 3: Injury
injury, accident, head trauma, pedestrian safety, falls, fires/burns/scalds, electrocution, suffocation, guns/firearms, drowning, poisoning, neurotoxin, poison, air toxic, heavy metal, lead, mercury, asbestos, carbon monoxide, CO, volatile organic, VOC
Hypothesis 4: Asthma
asthma, air pollution, indoor air quality, IAQ, allergen, dust mite, cockroach, rodent, mouse, bioaerosol, mold/fungi/fungus, endotoxin, viral infection/virus/viral illness, bacteria, microbial products, hygiene, hygiene hypothesis, pregnancy, stress, maternal stress, crime/violent crime/crime rates
Hypothesis 5: Obesity and physical development
obesity, urban sprawl, parks, recreation, walking, safety, endocrine disruptors
Other Miscellaneous search terms:
noise, zoning

Search terms were developed by the project team and were augmented by a technical information specialist to include plurals, root terms, alternative spellings, and synonyms. Terms were combined using Boolean AND/OR/NOT logic. In addition, neighborhood/community/housing terms were included, with variants and plurals: housing, home, house, or resident (to pick up residence, residential, etc.), community, neighborhood, housing characteristics, built environment, urban health. Other terms were added for each hypothesis.

Years included in the search were limited to 1999 through the present.

2.2 CRITERIA FOR RELEVANT STUDIES

Using this search strategy, up to several hundred potential articles were identified for each of the five hypotheses. Thus, due to the extensive nature of the literature, and recognizing time and resource constraints, coverage of all possible relevant topics describing potential cofactors in housing conditions was impossible.

To meet the objectives of this study, we were most interested in literature that provided information on:

> 1) Direct relationships between **measures of housing/neighborhood quality AND the five core NCS hypotheses**/health outcomes, OR

2) Relationships between **measures of housing/neighborhood quality AND physical, chemical or biological exposures/conditions of concern** (i.e., exposures related to the five core NCS hypotheses/health outcomes).

Under the first criterion, literature was considered relevant if the study provided information on direct relationships between conditions in the home or neighborhood and relevant health outcomes. For example, an article describing the effects of safety devices in the home or sidewalks in a neighborhood on injury rates would be considered relevant. Preference was also given to articles or studies that focused on children's health/development or exposures of concern in residential and neighborhood environments.

Under the second criterion, literature was also considered relevant if the study provided information on indirect (i.e., mediated through the exposure) relationships between conditions in the home or neighborhood and exposures that would be relevant to the health outcomes. For example, an article describing the relationship between home dampness and mold/endotoxin/ allergen levels (i.e., exposures known or hypothesized to influence asthma) would be considered highly relevant. Other examples of relevant articles following the first criterion would include investigations of neighborhood locations (e.g., rural setting near agriculture) that might affect pesticide levels in a dwelling, or studies looking at housing type and age (e.g., older multi-unit inner city rental housing) and lead levels in dust in a child's bedroom.

The review included both review studies and primary studies with original data. The article discussions in the main body of this report indicate the type of study. In general, the review was also restricted to studies that focused on human exposures, except to provide background on exposures of concern and establish potential linkages between these exposures and particular health outcomes.

Abstracts were reviewed initially. If they were ambiguous or if they suggested the article was relevant, full articles were checked for relevance. The reference sections of studies or articles identified as potentially relevant for the NCS were examined for additional relevant articles and studies. These referenced articles and studies were then obtained and reviewed for relevance. Due to resource constraints, however, an exhaustive review of all available literature was not conducted. As requested by the Work Assignment Officer, although the focus of the review was on literature published from 1999 to the present, if these papers referenced older works with widely accepted or validated results, they were also included.

Following the recommendations of the Work Assignment Officer, searches were not focused on socioeconomic status (SES) factors as main effects. Nonetheless, we have discovered that SES cannot be totally eliminated as a covariate, confounding variable, or intervening variable in the etiology of health outcomes for which housing factors are main effects or significant interacting effects. Therefore, in selecting relevant literature we have attempted to disregard articles that focus uniquely on SES, but include those where the SES role appears to be a secondary or contributory factor.

Articles that were deemed to be relevant were reviewed for this report and entered into a ProCite database designed for reference management. For maximum utility as a searchable database

resource for the NCS, each article was also tagged with keywords to link it to one or more of the key hypotheses.

In addition to the results of the literature searches, a substantial number of relevant references from other sources were also included in the ProCite database, such as bibliographies from National Center for Healthy Housing reports, Collaborative on Health reports, HUD Healthy Homes Initiative papers, materials from the NCS website (e.g., workgroup proceedings), and other HUD and NCS white papers. Several references were also added and reviewed at the recommendation of key experts in the housing and public health fields.

2.3 ORGANIZATION OF RESULTS

The discussion of the literature search results in Section 3 of this report follows in the most general sense the five core hypotheses proposed for the NCS, as follows:

- Hypothesis 1: Pregnancy and Birth Outcomes (see Section 3.1)
- Hypothesis 2: Neurobehavioral/Neurodevelopmental/Psychiatric Outcomes (see Section 3.2)
- Hypothesis 3: Injury (see Section 3.3)
- Hypothesis 4: Asthma (see Section 3.4)
- Hypothesis 5: Obesity and Development (see Section 3.5)

Each section discusses, for a given core hypothesis/health outcome, the literature relevant to housing/neighborhood quality and physical, chemical, or biological exposures/conditions of concern for that particular core hypothesis. Within each core hypothesis section, the discussion is divided, as appropriate, into a maximum of six subsections reflecting different broad sets of risk factors associated with housing and neighborhoods, including:

- General Housing/Neighborhood Quality
- Structural/Physical Risk Factors
- Chemical Risk Factors
- Biological Risk Factors
- Neighborhood Risk Factors/Other External Factors Affecting Housing
- Socioeconomic and Behavioral Co-factors.

Each of these subsections may also be further divided. For example, a subsection discussing literature found on chemical risk factors associated with housing/neighborhood environments may be divided into: pesticides, other organic chemicals (VOCs, formaldehyde, urea foam insulation, synthetic wood paneling, persistent bioaccumulative toxics, etc.), combustion by-products, lead, asbestos/fiberglass, and other inorganic chemicals (e.g., arsenic, chromium, copper, etc.).

Tables are included in each core hypothesis section presenting an overview of the body of literature found, followed by analysis of key individual articles.

3.0 RESULTS

3.1 LITERATURE ON THE RELATIONSHIPS BETWEEN HOUSING AND NEIGHBORHOOD CHARACTERISTICS AND PREGNANCY OUTCOMES

3.1.1 Additional Information on the Literature Review Approach for Pregnancy Outcomes

Hypothesis 1 of the National Children's Study addresses undesirable pregnancy outcomes including preterm birth and birth defects (see Appendix A). One of the sub-hypotheses under Hypothesis 1 (sub-hypothesis 1.2) is potentially related to housing and neighborhood characteristics – it tests whether intrauterine exposure to mediators of inflammation due to infection of vaginal, cervical, or uterine sites, or more distal sites (e.g., periodontal disease) is associated with an increased risk of preterm birth. The other sub-hypotheses related to undesirable pregnancy outcomes are not tied to housing or neighborhood characteristics or conditions.

Based on the results of a review study, Andrews et al. (2000) estimate that approximately 2% of pregnant women contract an intrauterine infection. Both uterine infections (Meis et al., 1995; Andrews et al., 2000) and other types of infections (Goldenberg et al., 2000) have been implicated as key components in many spontaneous preterm births. Preterm birth is defined as gestation less than 37 weeks. Preterm birth is a leading cause of infant mortality, and is also associated with nearly half of all congenital neurological defects (e.g., cerebral palsy) (Goldenberg and Rouse, 1998). Although gestational age at birth may be readily estimated in most cases, gestational age is uncertain in some pregnancies. In these cases, low birth weight (traditionally defined as less than 2,500 grams) may serve as a surrogate measure for preterm birth. Low birth weight may be a result of shortened gestation (<37 weeks), as well as inadequate fetal growth. However, for the purposes of this literature review, both preterm birth and low birth weight were included in the search terms of interest.

Although Hypothesis 1.2 as currently drafted focuses only on maternal infection as a risk factor in preterm birth, this literature review was conducted with a broader scope. The literature search strategy used also allowed for the inclusion of other housing and neighborhood risk factors that were reported in the literature to be associated with preterm birth or low birth weight, e.g., smoking in the home, ambient air pollution, exposure to toxins, etc.

3.1.2 Overview

According to 2002 birth statistics from the CDC, approximately 12.1 percent of children in the general U.S. population were born preterm, and 7.8 percent were born at low birth weight (Martin et al., 2003). These rates both represent increases from previous years, with the proportion of preterm infants rising 14 percent since 1990, and the percent born at low birth weight being at the highest level reported in more than three decades (Martin et al., 2003). Although these increases are influenced in part by the rising rates of multiple births (multiples are more likely to be born early and of low birth weight), the causes are not fully understood (Martin et al., 2003).

Associations between maternal behaviors during pregnancy – such as smoking and alcohol use – and low birth weight/preterm birth, as well as a plethora of other birth/health outcomes (e.g., mental retardation), have been well documented (Office of the Surgeon General, 2001; Kleinman and Madans, 1985; Sampson et al., 1994; Ventura et al., 2003; Roeleveld et al., 1992). For example, tobacco use during pregnancy has been clearly associated with low birth weight, as well as other adverse health outcomes such as intrauterine growth retardation, miscarriage, infant mortality, and later impaired child development with increased risks of behavioral disorders in childhood (Cnattingius, 2004; Office of the Surgeon General, 2001; Kleinman and Madans, 1985; Roeleveld et al., 1992). In 2002, 12.2 percent of mothers who smoked had a low birth weight child compared with 7.5 percent of nonsmokers (Martin et al., 2003). However, although we acknowledge that maternal smoking (and presumably the presence of any smokers in near proximity to the mother) and alcohol consumption are likely to be key predictors of preterm birth/low birth weight, the current focus of this literature review was primarily limited to non-behavioral factors in the home and neighborhood environment that may influence adverse pregnancy outcomes, including structural, biological, and chemical hazards. An overview of the literature found regarding these hazards is presented in Table 3.1-1 below.

Table 3.1-1. Summary of Key Literature Found on Housing/Neighborhood Characteristics Associated with Adverse Pregnancy/Birth Outcomes

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
GENERAL STUDIES AND REVIEWS		
General Housing		
General Neighborhood	While individual and neighborhood-level risk variables explain about an equal amount of variance in term low birth weight, only the neighborhood-level variables are significant predictors of preterm low birth weight	English et al. 2003
	Neighborhood-level risk factors have direct associations, as well as interactions with individual-level variables, in explaining low birth weight; individual-level risk factors for low birth weight behave differently depending upon the characteristics of the neighborhood of residence	O'Campo et al. 1997
	Living in neighborhoods that are less socioeconomically advantaged may influence birth weight; this influence may depend on maternal ethnicity	Pearl et al. 2001
	Neighborhood factors, including median household income, proportion of African-American residents, and rates of male unemployment, are related to preterm birth, but the mechanisms linking local environments to maternal risk remain to be specified; associations are non-linear and vary with race/ethnicity	Pickett et al. 2002
HYPOTHESIZED STRUCTURAL/PHYSICAL RISK FACTORS		
Housing type and age		
Structure, construction, condition		
Electrical system		
Fire Related Factors		
Building Materials		
HVAC		
Moisture		
Cleanliness		
Safety devices		
HYPOTHESIZED CHEMICAL RISK FACTORS		
Pesticides	Indoor pesticide usage is considerable in low-income, inner-city areas; approximately 70% of pregnant women in study cohort were exposed to pesticides	Berkowitz et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	during pregnancy; no clear associations were found between questionnaire data and urinary pesticide metabolite levels	
	Strong associations exist between dilapidated housing and pesticide exposures; Pesticide use in minority communities is widespread, with 85% of women reporting pest control activities during pregnancy	Whyatt et al. 2002
	High degree of correlation exists between maternal pesticide levels and levels found in cord blood samples, indicating that exposures are easily transferred between mother and fetus	Whyatt et al. 2003
	Highly significant associations exist between birth weight and length and blood cord levels of chlorpyrifos and diazinon; there is a significant decrease in exposure levels and increase in infant birth weight following EPA phase-out of residential use of these pesticides	Whyatt et al. 2004
	Maternal chlorpyrifos exposure is associated with reduced birth weight and length among African-American newborns	Perera et al. 2003
Other organic chemicals	High prenatal exposure to PAHs is associated with significantly lower birth weight and smaller head circumference	Perera et al. 2003
	Associations exist between personal PAH exposure and questionnaire variables including time spent outdoors, residential heating, and indoor burning of incense	Tonne et al. 2004
	Living near a PCB-contaminated site poses a statistically significant risk of giving birth to an infant of low birth weight	Baibergenova et al. 2003
	Adverse pregnancy outcomes, including spontaneous abortion, stillbirth, and preterm birth, are significantly higher among women chronically exposed to arsenic through drinking water compared to women who were not exposed	Ahmad et al. 2001
	Maternal exposure to elevated levels of TTHM and chloroform is associated with reductions in mean birth weight; an exposure-response relationship has been observed between risk of SGA and TTHM exposure	Wright et al. 2004
Combustion by-products	While severe CO poisoning poses serious short and long-term fetal risk, mild accidental exposure is likely to result in normal fetal outcome (excluding assessment of birth weight effects)	Koren et al. 1991
Lead	Effects of prenatal lead exposure may extend into later life and must be further investigated as risk factors for adult psychiatric diseases, such as schizophrenia	Opler et al. 2004
	Interaction between lead exposure and stress in pregnant females may permanently elevate corticosterone levels in offspring; such increases could suggest a new mechanism by which lead exposure could enhance susceptibility to diseases, dysfunctions, and deficits	Cory-Slechta et al. 2004
Asbestos, fiberglass		
Other inorganic chemicals		
Also see "Ambient air pollution" and "Traffic" under External Factors Affecting Housing		
HYPOTHESIZED BIOLOGICAL RISK FACTORS		
Multiple allergens	Mothers exposed to high concentrations of cat (but not dust mite) allergens during pregnancy have serum antibodies that can be freely transferred to the infant and might influence antibody production in the child	Platts-Mills et al. 2003
Dust mites		
Cockroaches		
Other insects (ticks, fleas, mosquitoes)		
Mice		
Rats		
Other rodents		
Molds		
Pets		

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Bacteria, endotoxins, microbial VOCs (mVOCs)	No association exists between bacterial vaginosis infection rates and SES characteristics in black or white women, with the exception of "absence of a home telephone"	Meis et al. 2000
	Bacterial vaginosis infections during pregnancy are a known risk factor for preterm birth	Meis et al. 1995
Other triggers (e.g., viral agents)	Prenatal infective complications may contribute to later development of asthma in children; flu and fever episodes during pregnancy are significantly associated with subsequent asthma development	Calvani et al. 2004
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS		
Location	Social decline and moving to an urban municipality (from a rural area) are associated with preterm delivery	Basso et al. 1999
	Low birth weight is associated with the area of total crop production within a 300-m zone around the mothers' residences; low birth weight was associated particularly with sugar beet and corn production zones	Xiang et al. 2000
	Living in a zip code district that is near a PCB-contaminated site poses a risk of giving birth to an infant of low birth weight	Baibergenova et al. 2003
	Prevalence of preterm birth is significantly higher in mothers living near oil refinery plants than in control mothers	Yang et al. 2004
Zoning/building codes		
Ambient air pollution	A significant relationship exists between pregnancy outcomes (preterm birth) and ambient air pollution due to close proximity to oil refinery facilities in Taiwan	Yang et al. 2004
	Risk of low birth weight and preterm birth increases by approximately 10-20% among infants born to women living close to heavy-traffic roadways, with stronger effects observed for women whose third trimesters fall during fall/winter months, who live in high background air pollution areas, and/or who live in more impoverished areas	Wilhelm and Ritz 2003
	Exposure to air pollution during pregnancy may interfere with weight gain in the fetus; effect may be most robust for carbon monoxide, followed by PM_{10}	Gouveia et al. 2004
	Relatively low concentrations of gaseous air pollutants may be associated with adverse effects on birth outcomes	Liu et al. 2003
	Risks for low birth weight tend to increase with exposure to air pollutants during early to mid-pregnancy	Lee et al. 2003
	Exposure to higher levels of ambient carbon monoxide during the last trimester of pregnancy is associated with a significantly increased risk of low birth weight	Ritz and Yu 1999
Traffic	Risk of low birth weight and preterm birth is increased in infants born to women living close to high-density traffic roadways, and therefore potentially exposed to higher levels of motor vehicle exhaust	Wilhelm and Ritz 2003
Noise	Although higher chronic physiological stress arousal is observed in subjects exposed to traffic noise compared to those less exposed, it is unknown whether these physiological responses would translate to prenatal stress or result in adverse birth outcomes	Babisch et al. 2001
	No strong evidence has been found linking noise exposure to low birth weight or congenital birth defects, though noise related stress has been linked to hypertension, psychological symptoms, and impaired reading comprehension and long-term memory	Stansfeld et al. 2000
Crime rates, violence, neighborhood safety	Unfavorable perceptions of their residential environment by mothers, in terms of police protection, personal safety, cleanliness, etc., is associated with very low birth weight infants; frequency of stressful life events is also associated with very low birth weight	Collins et al. 1998
Recreational facilities, playground equipment		
Pedestrian and bicycle access		
Water hazards		

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
HYPOTHESIZED BEHAVIORAL & SES RISK FACTORS		
SES mediators	Dental caries in Brazilian adolescents are influenced by socioeconomic factors in early life	Nicolau et al. 2003
Other behavioral factors	Maternal stress has been linked to preterm delivery or low birth weight in U.S. studies of economically deprived African-American women and in European studies; findings from European studies are sometimes conflicting because they combine preterm delivery and low birth weight outcomes	Austin 2000
	Maternal stress may increase certain hormones leading to increased uterine contractility, or it may increase cytokine production (which independently may lead to preterm birth or increase susceptibility to infection, thereby increasing risk of preterm birth); stress may change maternal health behaviors that lead to preterm birth	Gennaro and Hennessy 2003
	Maternal exposure to three or more stressful life events during pregnancy increases risk of low birth weight infants	Collins et al. 1998
	Stress is significantly associated with spontaneous preterm birth and low birth weight; no other psychosocial status indicators studied (including anxiety, self-esteem, and depression) are significant predictors of preterm birth or low birth weight	Copper et al. 1996

Although it is hypothesized that certain housing and neighborhood characteristics could potentially influence maternal infections (and thus preterm birth), as shown in Table 3.1-1, this literature search uncovered no literature elucidating possible linkages between specific housing/neighborhood characteristics or conditions and maternal infections leading to adverse pregnancy outcomes, or even maternal infection rates in a general sense. One study was identified that examined potential factors affecting the number of dental caries in adolescents, and one study was found that looked at bacterial vaginosis rates in pregnant women – as discussed below, both of these studies were primarily linked to socioeconomic status (SES) effects. Another article provided evidence that prenatal infective complications may contribute to subsequent asthma development in children, though the study did not discuss potential housing or neighborhood-related causes of infections (Calvani et al., 2004). Additional information is needed regarding this potential linkage.

A modest body of research was found to exist, however, on the relationships between adverse pregnancy outcomes/low birth weight and chemical exposures (e.g., pesticides, PCBs, and air pollution), neighborhood characteristics, and other conditions leading to general maternal stress.

The following sections detail the literature found on specific housing and neighborhood related risk factors for adverse pregnancy outcomes.

3.1.3 Chemical Attributes of Housing/Neighborhoods Associated with Adverse Pregnancy Outcomes

In the literature, several types of chemical exposures were found to be linked to housing and neighborhood factors and adverse pregnancy outcomes. These include exposures to commonly used pesticides around the home, organic chemicals (PCBs, PAHs), and indoor/outdoor air pollution.

Pesticides. The use of pesticides is widespread in the United States, particularly in agricultural settings, though use in home and garden applications is on the rise. Some research indicates that pesticides are of particular concern in low-income, inner-city areas, where conditions favor pest infestation and, consequently, pesticide usage (Berkowitz et al., 2003). Efforts are underway to assess the degree of residential pesticide use in the U.S. and effects of exposure, particularly upon children and pregnant women. As concerns with pesticide exposures are predominantly associated with children's neurobehavioral and neurodevelopmental outcomes in the literature, detailed information on pesticide use and storage patterns in the home, as well as additional adverse health effects for children, is included in Section 3.2 of this report. Several studies were found in this literature search that specifically investigated pesticide exposures during pregnancy, as discussed below.

To investigate the relationship between prenatal exposure to indoor pesticides and infant growth and development, Berkowitz et al. (2003) conducted a prospective, multiethnic cohort study of mothers and infants delivered at Mount Sinai Hospital in New York City. Preliminary results based on questionnaire items and analysis of maternal urinary metabolite levels among 386 women indicated that indoor pesticide use was considerable, with approximately 70% of women estimated to be exposed to indoor pesticides during pregnancy. Commonly detected pesticide metabolites were assessed in urine, including trichloro-2-pyridinol or TCP (a metabolite of chlorpyrifos), phenoxybenzoic acid (PBA) metabolites of several pyrethroid insecticides (one, sumuthrin was used to spray against the West Nile virus in 2000), and pentachlorophenol (PCP). PCP was a widely used wood preservative until the 1970s. Questionnaires administered in the study also helped to elucidate some behavioral and housing factors associated with exposures. Nearly half (47.9%) of those interviewed reported having an insect problem, and 27.5% reported having a rodent problem. Close to half reported applying (or another household member applying) pesticides during the pregnancy, including bait traps, can sprays, gels, boric acid, sticky traps, pest bombs, and other miscellaneous products. However, no clear associations were observed between questionnaire data (including SES and building characteristics information) and urinary metabolites. Temporal trends in PBA metabolites were observed, consistent with seasonal pyrethroid spraying in the city.

In an ongoing study being conducted by Columbia University on the effects of indoor air pollutants on pregnant women and their newborns in minority communities within the New York City area, strong associations were observed between dilapidated housing and pesticide exposures. Results suggested widespread use of pesticides in these areas, with 85% of the women reporting the use of pest control techniques during pregnancy, and at least four pesticides detected in the personal air samples of all women who consented to monitoring during their third trimester (Whyatt et al., 2002). The project also reported a high degree of correlation between maternal pesticide levels and levels found in cord blood samples, indicating that exposures are easily transferred between mother and fetus (Whyatt et al., 2003). Most recently, the study found highly significant associations between birth weight and length and blood cord levels of chlorpyrifos and diazinon (n = 314 mother-newborn pairs) (Whyatt et al., 2004). Among newborns born after the EPA regulatory actions to phase out residential use of these insecticides in 2000-2001, exposure levels were substantially lower, and significant increases in infant birth weights were observed (Whyatt et al., 2004).

In another study of prenatal exposure to common urban pollutants, maternal chlorpyrifos exposure was associated with reduced birth weight and length among African-American newborns (263 nonsmoking African-American and Dominican women), as assessed by personal monitoring, biomarkers, questionnaire data, and medical records, after controlling for the effects of other known physical, biologic, and toxic determinants of fetal growth (Perera et al., 2003).

Other Hazardous Chemicals. Although the role of other organic chemicals in children's neurodevelopmental health is increasingly recognized in the literature (see Section 3.2 of this report), only limited information appeared to be available on prenatal exposures to these contaminants. A majority of the research found in this literature search on pregnancy outcomes and toxic exposures focused on ambient air pollution, which includes a mixture of toxics – some organic and some inorganic combustion-related toxics. Research regarding pregnancy outcomes and combustion-related air toxics (e.g., nitrogen dioxide, carbon monoxide, particulate matter) is discussed in Section 3.1.5 of this report on neighborhood factors. Literature found on exposure to other organic and inorganic chemicals — including PAHs, PCBs, arsenic, and lead — during pregnancy is discussed below.

In a study by Perera et al. (2003), exposures to polycyclic aromatic hydrocarbons (PAHs), which are a common class of organic urban air pollutants (and one of many found in particulate matter from combustion sources), were monitored during pregnancy by personal air sampling involving 263 nonsmoking African-American and Dominican women in New York City. Among African-Americans, high prenatal exposure to PAHs was associated with significantly lower birth weight and smaller head circumference, after adjusting for potential confounders. The authors report that these findings are consistent with studies showing associations between ambient air pollution and low birth weight (Perera et al., 2003). In a cohort of 348 pregnant women in New York City, Tonne et al. (2004) measured personal exposures to PAHs and attempted to identify any associations with socioeconomic factors, day-to-day activities, or other environmental exposures for which information was collected via questionnaire. Analysis revealed associations between personal PAH exposures and several of the questionnaire variables, including time spent outdoors, residential heating, and indoor burning of incense.

Baibergenova et al. (2003) also investigated low birth weight and organic chemical exposures, this time as a result of proximity to industrial waste sites. According to the authors, the literature has shown an association between a mother's residence being near a hazardous waste site and adverse birth outcomes in some, but not all, past studies. Based on previous research indicating that women exposed to polychlorinated biphenyls (PCBs) are at increased risk of giving birth to an infant with low birth weight, Baibergenova et al. (2003) focused on residential proximity to waste sites contaminated with PCBs. By identifying 187 zip codes in New York State that contained or abutted PCB-contaminated sites (Superfund sties, National Priority List sites, and Areas of Concern) and comparing this data to maternal place of residence (based on zip codes from the state vital statistics records) for all births between 1994 and 2000, the authors found the data supported the hypothesis that living in a zip code near a PCB-contaminated site poses a risk of giving birth to an infant of low birth weight. After adjusting for sex of the infant, mother's age, race, weight, height, education, income, marital status, and smoking, there was still a statistically significant 6% increased risk of giving birth to a male infant of low birth weight.

In addition to airborne exposure, some studies have looked at maternal exposure to toxics through drinking water. Ahmad et al. (2001) studied a group of women of reproductive age (15-49 years) in Bangladesh, India, who were chronically exposed to arsenic through drinking water. In comparison to women who were not exposed, adverse pregnancy outcomes, including spontaneous abortion, stillbirth, and preterm birth, were significantly higher in the arsenic-exposed group. Rates of spontaneous abortion, stillbirth, and preterm birth were 2.9, 2.24, and 2.54 times higher, respectively, in the exposed group than in the non-exposed group. In another study of maternal drinking water exposures during pregnancy, Wright et al. (2004) used birth certificate data on 196,000 infants to examine the effect of town-average concentrations of total trihalomethane (TTHM) and chloroform, which are two water disinfection by-products, in 109 towns in Massachusetts in relation to mean birth weight, mean gestational age, small for gestational age (SGA) infancy, and preterm delivery. They observed reductions in mean birth weight (12-18 g) for maternal trihalomethane exposures above the 90th percentile compared with those below the 50th percentile. Birth weight reductions were detected for chloroform exposures greater than 20 μg/L and TTHM exposures greater than 40 μg/L. Elevated trihalomethanes were associated with increases in gestational duration and a reduced risk of preterm delivery, however, which was consistent with observations of an exposure-response effect of trihalomethanes for risk of SGA. Elevated mutagenic activity was associated with SGA in this study.

It has been well established that exposure to residential lead hazards is a serious health concern for children. In this literature search, a few articles were also found that investigated the effects of prenatal lead exposure. Opler et al. (2004) studied potential linkages between environmental lead exposure during prenatal development and later development of schizophrenia using archived serum samples from a cohort of live births in Oakland, California between 1959 and 1966. Serum analyses showed elevated levels of a biologic marker of lead exposure (delta-ALA) in numerous samples, with an odds ratio for schizophrenia associated with the highest category (equivalent to a blood lead level greater than or equal to 15 ug/dL) of 2.43 (95% CI, 0.99-5.96; $p = 0.051$). These findings suggest that the effects of prenatal lead exposure may extend into later life and must be further investigated as risk factors for adult psychiatric diseases.

As lead is known to often be a particular risk for lower SES, inner-city children (e.g., due to older, dilapidated housing), Cory-Slechta et al. (2004) conducted a study on potential interactions between lead and another risk factor known to affect low SES women – stress. Using a rodent model and measuring corticosterone, a hormone linked to chronic stress response, the researchers tested the hypothesis that these co-occurring risk factors, lead exposure and environmental stress, would interact and modulate each others' effects. Results showed that lead plus stress in pregnant females permanently elevated corticosterone levels in offspring, even when lead exposures were short-term. The authors suggest that such increases could indicate a potential new mechanism by which lead exposure could directly or indirectly enhance susceptibility to diseases and dysfunctions and induce cognitive deficits. Moreover, the interactive effects of lead and stress, and particularly the potentiated effects of lead plus stress, raise questions about whether current risk assessment strategies sufficiently consider the true cumulative risk of inner-city lead exposures.

Combustion By-Products. This literature search also uncovered studies relating prenatal exposure to combustion by-products, including carbon monoxide (CO) and nitrogen dioxide (NO_2), to low birth weight and other fetal abnormalities. The majority of these (Gouveia et al., 2004; Liu et al., 2003; Lee et al., 2003; Ritz and Yu, 1999) specifically addressed ambient levels of combustion-related air pollution and low birth weight, and thus are discussed in Section 3.1.5 of this report on neighborhood factors. Koren et al. (1991), however, conducted a prospective, multicenter study of acute housing-related carbon monoxide (CO) poisoning occurring in pregnancies between December 1985 and March 1989. The sources of CO were malfunctioning furnaces (n = 16), water heaters (n = 7), car fumes (n = 6), and methylene chloride inhalation (n = 3). Severe toxicity incidents resulted in three cases of adverse pregnancy outcomes (including two stillbirths and one case of cerebral palsy), as well as two cases of severe toxicity with normal outcomes following hyperbaric oxygen therapy. Cases of mild or moderate CO poisoning (31 babies) exhibited subsequent normal physical and neurobehavioral development. The authors concluded that while severe CO poisoning poses serious short- and long-term fetal risk, mild accidental exposure is likely to result in normal fetal outcome, although birth weight effects were not assessed.

3.1.4 Biological Attributes of Housing Associated with Adverse Pregnancy Outcomes

As mentioned previously, no literature was found relating any biological exposure or other housing/neighborhoods conditions to maternal infections leading to adverse pregnancy outcomes, or even infection rates in a general sense. Several studies (Stark et al., 2003; Belanger et al., 2003; Gent et al., 2002; see Section 3.4.5 on biological factors in respiratory outcomes) were identified that found higher fungal levels in homes to be related to infections of the lower respiratory tract in children, but whether these studies would transfer to an adult is unknown.

One study was identified that investigated numerous social and biological factors that might affect levels of dental caries in Brazilian adolescents (Nicolau et al., 2003). Results indicated that dental caries in adolescents were influenced by socioeconomic factors in early life.

Regarding maternal infections, Meis et al. (2000) examined the relationship between SES and bacterial vaginosis infections during pregnancy, which are a known risk factor for preterm birth (Meis et al., 1995). The study evaluated data from the Preterm Prediction Study of 2,929 women prospectively followed during their pregnancies. Analyses found no association between bacterial vaginosis infection rates and SES characteristics in either black or white women (with the sole exception of "absence of a home telephone").

Non-infectious biological exposures of pregnant women were investigated by Platts-Mills et al. (2003), who conducted a study on maternal immune responses to cat and mite allergens during pregnancy and passive transfer of immune response to fetus. In the study of 465 mothers, 424 infants, and 230 children to age 3, a significant proportion (approximately 15%) of mothers exposed to high concentrations of cat (but not mite) allergens had serum antibodies that could be freely transferred to the infant and might influence antibody production in the child. The authors suggest that these results raise questions about the independent role of the mother, and exposures the mother receives during pregnancy, in the inheritance of allergy. As discussed above, one

article was identified that provided evidence that prenatal infective complications may contribute to the later development of asthma in children, although potential housing or neighborhood related causes of the infection were not discussed (Calvani et al., 2004). In this study of 338 children with asthma and 467 controls, flu and fever episodes during pregnancy (mainly episodes contracted during the third trimester) were observed to be significantly associated with the later development of asthma in children.

3.1.5 Neighborhood Attributes and Other External Factors Affecting Housing Associated with Adverse Pregnancy Outcomes

General Neighborhood. Neighborhood attributes investigated in the literature in association with preterm birth/low birth weight included location, ambient air pollution, traffic, and neighborhood crime rates and perceived safety. Several studies on general, cumulative effects of neighborhoods have also been conducted. English et al. (2003) attempted to compare the relative importance of neighborhood risk factors with individual-level risk factors in predicting changes in two measures of adverse reproductive health – term and preterm low birth weight. The researchers analyzed birth data in San Diego County, California, for approximately 16,000 births in 1980 and 24,000 births in 1990 and identified several statistically significant "hot spots" of elevated risk for low birth weight. Comparing this information with neighborhood- and individual-level data, the authors found that while individual- and neighborhood-level variables explained about an equal amount of variance in term low birth weight, only the neighborhood-level variables were significant predictors of preterm low birth weight. O'Campo et al. (1997) also attempted to assess the contribution of macrolevel social factors on low birth weight in Baltimore, Maryland, by linking census tract-level data on social stratification, community empowerment, and environmental stressors to birth certificate records. Individual-level factors assessed included maternal education and age, medical assistance health insurance (Medicaid), and trimester of prenatal care initiation; and neighborhood-levels factors included ratio of homeowners to renters, rate of housing violations, community crime rates, and per capita income. Analyses indicated that neighborhood-level factors had direct associations, as well as interactions with individual-level variables in explaining low birth weight. Most notably, all of the individual risk factors also appeared to have significant interaction with neighborhood-level variables; that is, individual-level risk factors for low birth weight behaved differently depending upon the characteristics of the neighborhood of residence. For example, women living in high-risk neighborhoods benefited less from prenatal care than did women living in lower-risk neighborhoods.

Location. Place of residence has been shown to be related to numerous health outcomes, including adverse pregnancy outcomes. Location factors reported in the literature included setting (e.g., rural, urban, or suburban), proximity to agricultural activities, and proximity to industry or hazardous waste sites.

Social decline and moving to an urban municipality (from a rural area) were associated with preterm delivery in a national cohort of women (Basso et al., 1999). In another study focused on rural areas, Xiang et al. (2000) used geographic information system (GIS) technologies to identify the proximity of maternal residence to agricultural areas and evaluate the association between crop production patterns around mothers' residences and low birth weight for 125 births in Weld County, Colorado. Results of the analysis indicated that low birth weight was

associated with the area of total crop production within a 300-m zone around the mothers' residences. In particular, low birth weight was associated with sugar beet production and corn production zones.

As mentioned previously, Baibergenova et al. (2003) investigated low birth weight in relation to proximity to industrial waste sites contaminated with PCBs. Data from this study supported the hypothesis that living near a PCB-contaminated site poses a risk of giving birth to an infant of low birth weight. Yang et al. (2004) also conducted a study to examine the relationship between pregnancy outcomes and proximity to industrial activities. Specifically, the researchers looked at residences near petrochemical and petroleum (oil refinery) industries in Taiwan, which are two of the main sources of industrial air pollution in this region. Data showed that the prevalence of preterm birth was significantly higher in mothers living near the oil refinery plants than in control mothers.

Ambient Air Pollution. The association between ambient air pollution and adverse birth outcomes has been investigated in the literature in several studies. As discussed above, Yang et al. (2004) observed a significant relationship between pregnancy outcomes (preterm birth) and ambient air pollution due to close proximity to oil refinery facilities in Taiwan. One known dominant source of ambient air pollution in cities, automobile traffic, was also specifically examined by Wilhelm and Ritz (2003) in relation to the risk of term low birth weight and preterm birth. Results of the study, conducted over a two-year period in Los Angeles County, California, revealed an approximate 10-20% increase in risk of low birth weight and preterm birth in infants born to women living close to heavy-traffic roadways. Stronger effects were observed for women whose third trimesters fell during fall/winter months, who lived in high background air-pollution areas, and/or who lived in more impoverished areas. The majority of ambient air quality studies identified in this literature search, however, tended to focus on measurements of specific air toxics. Specific components of air pollution most commonly assessed in the literature include carbon monoxide, sulfur dioxide, nitrogen dioxide, and particulate matter less than ten micrometers in diameter.

The association between exposure to outdoor air pollution during pregnancy and subsequent infant birth weight was recently explored by Gouveia et al. (2004) in a study of all singleton full term live births in Sao Paulo, Brazil during a one year period. Birth data was compared to measured daily mean levels of particulate matter (PM_{10}), sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone over a one year period. Data indicated that exposure to air pollution during pregnancy may interfere with weight gain in the fetus. Of the toxic air components measured, this effect appeared to be most robust for carbon monoxide, followed by PM_{10}. For each 1-ppm increase in mean exposure to carbon monoxide during the first trimester, a reduction of 23 g in birth weight was estimated.

Liu et al. (2003) looked at potential associations between ambient air pollution and preterm birth, low birth weight, and intrauterine growth retardation (IUGR) among singleton live births in Vancouver, Canada, for 1985-1998. Specific air pollution components measured included sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone. The investigation indicated that relatively low concentrations of gaseous air pollutants may be associated with adverse effects on birth outcomes: low birth weight was associated with exposure to SO_2 during

the first month of pregnancy; preterm birth was associated with exposure to SO_2 and to CO during the last month of pregnancy, and IUGR was associated with SO_2, NO_2, and CO exposure during the first month of pregnancy.

Lee et al. (2003) conducted a similar study on air pollution exposure levels and low birth weight in Seoul, Korea. Using monthly air pollution data to estimate exposures during each trimester, analyses suggested that the risks for low birth weight tended to increase with exposure to air pollutants during early to mid-pregnancy. Specifically, carbon monoxide exposure between months two and five of pregnancy, exposure to particulate matter (PM_{10}) in months two and four, and exposure to sulfur dioxide or nitrogen dioxide between months three and five all appeared to contribute to increased risks of low birth weight.

Maternal exposures to carbon monoxide in ambient air pollution were also studied by Ritz and Yu (1999) in a cohort consisting of 125,573 singleton births in Los Angeles, California. Data indicated that exposure to higher levels of ambient carbon monoxide (>5.5 ppm 3-month average) during the last trimester of pregnancy was associated with a significantly increased risk for low birth weight after adjustment for potential confounders, including commuting habits in the monitoring area; sex of the child; level of prenatal care; and age, ethnicity, and education of the mother.

Traffic. As discussed above, Wilhelm and Ritz (2003) found an increased risk of low birth weight and preterm birth in infants born to women living close to high-density traffic roadways, and therefore potentially exposed to higher levels of motor vehicle exhaust. Traffic density estimates in this study, however, reflect only the total number of vehicles passing by a residence and do not differentiate among gasoline and diesel-fueled vehicles, vehicle speeds, or the typical age of vehicles that frequent a given street. Also of note in this study, stronger effects were observed for women whose third trimesters fell during fall/winter months, who lived in high background air-pollution areas, and/or who lived in more impoverished areas. The authors suggest various factors that may help to explain some of this variability, including location effects and socioeconomic status. For example, as the amount of outdoor pollution penetrating indoors is a function of housing characteristics (including air exchange rates, building surface to volume ratios, use of air conditioning, and use of windows for ventilation), the authors hypothesize that greater use of open windows and doors in the relatively warm climate of the Los Angeles area, as well as poorer-quality housing (e.g., less tightly sealed windows, lack of air conditioning, and more open windows) in lower SES areas may result in greater penetration of traffic-related pollutants indoors. Alternatively, the authors also suggest that SES variability could be caused by greater vulnerability to air pollution exposures as a result of poor nutrition during pregnancy, increased reliance on public transit (resulting in higher commuter exposures), or because of a greater proportion of older, high-polluting vehicles on streets in these areas.

In addition to pollution-related exposures occurring as a result of proximity to traffic, researchers have also investigated the stress-related effects of excessive traffic noise, as discussed in Section 3.2.6 of this report, on behavioral and mental health outcomes. Although these studies have not focused specifically on maternal exposures to traffic noise as a stressor during pregnancy, general maternal stress has been linked (see section 3.1.6 below) to undesirable pregnancy outcomes. The traffic noise-stress linkage was examined by Babisch et al. (2001) in a study of

30 to 45-year-old women whose bedroom and/or living room were facing streets of varying traffic volume. Measurements of adrenaline and noradrenaline concentrations in urine were used as indicators of physiological stress. Although higher chronic physiological stress arousal was observed in noise-exposed subjects compared to those less exposed, whether these physiological responses to noise would translate to prenatal stress or result in adverse birth outcomes is unknown. In a review study conducted by Stansfeld et al. (2000), stress related to traffic noise — as well as other noise — was linked to hypertension in occupational studies, and stress was linked to psychological symptoms, impaired reading comprehension and long-term memory, and possibly increased blood pressure in community studies; however, the authors found no strong evidence from carefully controlled studies that noise exposure is related to low birth weight or to congenital birth defects.

Neighborhood Social Environment. The relationship between birth outcomes and neighborhood social environment, including factors such as crime rates/neighborhood safety, median incomes, and unemployment rates, were also examined in several studies identified in this literature search.

Collins et al. (1998) conducted a study to explore the relation between a mother's perception of her own neighborhood and very low birth weight infants (defined as <1,500 g). In the study, 28 African-American mothers of very low birth weight infants were administered a questionnaire to rate their community, in term of police protection, protection of property, personal safety, friendliness, delivery of municipal services, cleanliness, quietness, and schools. Results of the questionnaire indicated that these mothers' perceptions of their residential environment were associated with very low birth weight infants, with the odds ratio for very low birth weight for mothers rating their neighborhood unfavorably ranging between 1.7 and 3.2. Frequency of stressful life events during pregnancy was also associated with very low birth weight in this study.

Relationships between low birth weight and another neighborhood characteristic, neighborhood SES, were also examined in several studies (Pearl et al., 2001; Pickett et al., 2002). In Pearl et al. (2001), neighborhood levels of poverty, unemployment, and education were compared to birth records of low birth weight among 8,457 women in five ethnic groups in California. After adjustments for the mother's individual socioeconomic characteristics, the analysis indicated that among blacks and Asians, low birth weight was associated with less-favorable neighborhood socioeconomic characteristics. The authors concluded that although living in neighborhoods that are less socioeconomically advantaged may influence birth weight, this influence may depend on maternal ethnicity. In Pickett et al. (2002), associations between neighborhood socioeconomic context and preterm delivery, independent of maternal and family SES, were explored in 417 African-American and 1,244 white women in San Francisco. Analyses of neighborhood socioeconomic contexts indicated that neighborhood factors and changes over time, including median household income, proportion of African-American residents, and rates of male unemployment, were associated with preterm delivery; but associations were non-linear and varied with race/ethnicity. The authors suggest that although these findings show that neighborhood factors are related to preterm birth, the mechanisms linking local environments to maternal risk remain to be specified.

3.1.6 Stress Mediators Associated with Adverse Pregnancy Outcomes

In addition to neighborhood stressors, individual-level maternal stress was examined in relation to adverse pregnancy outcomes in several studies identified in this literature search. Although the majority of these studies did not explicitly relate housing or neighborhood characteristics to maternal stress, these studies are noteworthy in the sense that many of the neighborhood studies discussed in previous sections of this paper were able to draw the linkages between neighborhood characteristics and stress (e.g., noise and stress, traffic and stress, crime and stress).

Two of the stress-related studies identified in this literature search were review studies. Austin (2000) conducted a review of the literature relating to maternal stress and obstetric outcomes, focusing on prospective studies that looked at epidemiological factors as well as physiological mechanisms. The Austin (2000) review found a number of U.S. studies that provided evidence of an association between maternal stress and preterm delivery in economically deprived African-American women, as well as numerous European studies (three large Scandinavian epidemiological studies) that also confirmed the linkage between maternal stress and preterm delivery or low birth weight. Austin notes, however, that the findings from the European studies are sometimes conflicting because they combine the preterm delivery and low birth weight outcome measures. Gennaro and Hennessy (2003) also evaluated the current research on stress and pregnancy outcomes, specifically the impacts of psychological and physiological maternal stress on preterm birth. The authors found that although research findings on the relationship between stress and preterm birth have been contradictory, some studies suggest maternal stress may increase certain hormones and that could result in increased uterine contractility, or that stress may increase cytokine production (which independently may lead to preterm birth or increase susceptibility to infection, thereby increasing the risk of preterm birth). Finally, in this review the authors found evidence that stress may change maternal health behaviors that lead to preterm birth.

Possible linkages between maternal stress and adverse pregnancy outcomes were also examined in two prospective, controlled studies identified in this literature search. In a survey of mothers of very low birth weight infants, Collins et al. (1998) (also discussed above in the "neighborhood social environment" section) found an increased risk of low birth weight infants for mothers exposed to three or more stressful life events during pregnancy. Finally, Copper et al. (1996) examined possible associations between various measures of poor psychosocial status (including anxiety, stress, self-esteem, and depression) in pregnancy and spontaneous preterm birth or low birth weight. Analyses of data collected for 2,593 women indicated that stress was significantly associated with spontaneous preterm birth and with low birth weight; however, none of the other psychosocial status indicators were significant predictors of preterm birth or low birth weight.

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3.2 LITERATURE ON THE RELATIONSHIPS BETWEEN HOUSING AND NEIGHBORHOOD CHARACTERISTICS AND NEUROBEHAVIORAL AND NEURODEVELOPMENTAL OUTCOMES

3.2.1 Additional Information on the Literature Review Approach for Developmental Disabilities, Neurobehavioral, and Neurodevelopmental Outcomes

Hypothesis 2 of the National Children's Study addresses altered neurobehavioral development, developmental disabilities, and psychiatric outcomes (see Appendix A). Specifically, Hypothesis 2.1 tests whether repeated low-level exposure to nonpersistent pesticides *in utero* or postnatally increases the risk of poor performance on neurobehavioral and cognitive examinations during infancy and later in childhood, and Hypotheses 2.2 and 2.3 test whether prenatal infection and mediators of inflammation are risk factors for neurodevelopmental disabilities (such as cerebral palsy and autism) or schizophrenia. A related core NCS area focusing on physical development, Hypothesis 5.7, tests whether *in utero* and subsequent exposure to environmental agents that affect the endocrine system (e.g., bisphenol A, atrazine, and lead) results in altered age at puberty. Literature found related to risk factors for altered physical development is discussed in section 3.5 of this report.

The primary outcomes of interest described in NCS core Hypothesis 2 are currently limited to poor performance on neurobehavioral and cognitive examinations, select neurodevelopmental disabilities, and schizophrenia. For the purposes of this literature review, the suite of outcomes was broadened even further to include any neurobehavioral or neurodevelopmental outcomes that were related in the literature to housing or neighborhood characteristics or exposures. General mental health outcomes were also included in the literature search.

In addition, although the exposures of focus in Hypothesis 2 as currently drafted are limited to nonpersistent pesticides, prenatal infection, and mediators of inflammation, the literature search strategy employed also allowed for the inclusion of additional housing and neighborhood risk factors that were reported in the literature to be associated with neurological or mental health outcomes, such as other chemical exposures (e.g., persistent pesticides, other organics, lead, etc.), mold, and community factors (e.g., crowding, stress).

3.2.2 Overview

Neurodevelopmental disabilities, such as dyslexia and other learning disabilities, attention deficit hyperactivity disorder, developmental delays, autism, and emotional and behavioral problems, affect millions of children in the United States (Landrigan et al., 2004; CDC/NCHS, 2004). For example, the Centers for Disease Control and Prevention estimated that for children between the ages of 3 and 17 in 2002, 4.9 million (8.1%) had a learning disability and 4.3 million (7.2%) had Attention Deficit Hyperactivity Disorder (ADHD). The percent of children with learning disabilities in families with annual incomes less than $20,000 was more than twice that of children in families with incomes of $75,000 or more (13% versus 6%). Also, compared with children with excellent or very good health, children with fair or poor health were more than five times as likely to have a learning disability (6% versus 34%) and four times as likely to have ADHD (6% versus 24%) (CDC/NCHS, 2004). The exact prevalence of autism is uncertain due to lack of surveillance, but 1 per 1,000 is the most frequently estimated rate in the literature (London and Etzel, 2000). Although some of these disabilities are due to known causes such as genetic disorders, chromosomal aberrations, perinatal meningitis, or exposure to drugs and alcohol *in utero*, the causes of most (e.g., over 75% per Weiss and Landrigan, 2000) neurodevelopmental disabilities remain unknown (Landrigan et al., 2004; Weiss and Landrigan, 2000). Researchers hypothesize that childhood neurodevelopment and brain function are the result of complex interactions among any number of genetic, environmental (toxicological), and social determinants (Goldman and Koduru, 2000).

A substantial body of research has provided evidence that some chemicals present in residential environments (e.g., lead and pesticides) can cause serious toxic effects to the nervous system of humans, with the potential to cause neurological disorders, such as cognitive impairment, behavioral disturbances (e.g., mood shifts, aggression), and impairment of memory. In recent years, research on children's exposures to neurotoxic substances has also proved that children are at a profoundly higher risk of poisoning by neurotoxicants than adults due to their lower body weights and differences between children and adults in their patterns of absorption, metabolism, and excretion of chemicals, as well as pathways and types of environmental exposures (NRC, 1993; Faustman et al., 2000). Studies indicate that the fetus, infant and older children are more sensitive than adults to low levels of many environmental toxicants due to developing organ systems (Faustman et al., 2000; EPA/OCHP, 2003). In particular, the developing neurological

system is especially vulnerable to damage from neurotoxicants – unlike other organ systems, the development of the central nervous system (CNS) has been shown to be unidirectional, which means that damage to the system at one developmental stage can cause permanent CNS alterations (Faustman et al., 2000). Full development of some areas of the brain (e.g., myelination of the nerve fibers) is not complete until adolescence (Bearer, 1995). In addition to developmental differences, children may also receive higher exposures to some neurotoxicants through food and their environment (i.e., per kilogram of body weight), and as a result of their behavior (e.g., play and mouthing behavior) (Natural Resources Defense Council, 1997; Olden and Guthrie, 2000). It is these unique exposure patterns and developmental characteristics that make children at special risk from exposures to neurotoxic substances, and which have prompted the children's environmental health field to embrace the paradigm that "children are not just small adults."

Research has also indicated that in addition to residential chemical exposures, the physical characteristics of the built environment itself can have direct and indirect effects on mental health. For example, high-rise housing can be an adverse environment for the psychological well-being of women with young children (Evans, 2003a). Evans (2003a) notes that in many studies poor-quality housing appears to increase psychological distress, but cites methodological issues as a barrier to drawing clear conclusions. Other housing factors cited as potentially elevating psychological distress include residential crowding (number of people per room), noise (e.g., airports, traffic), malodorous air pollutants, insufficient daylight, and unsafe neighborhoods.

An overview of the literature found regarding neurotoxic exposure hazards in residential environments, as well as other community factors involved in mental health outcomes, is presented in Table 3.2-1 below.

Table 3.2-1. Summary of Key Literature Found on Housing/Neighborhood Characteristics Associated with Neurobehavioral Development, Developmental Disabilities and Psychiatric Outcomes

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
GENERAL STUDIES AND REVIEWS		
General Housing		
General Neighborhood		
HYPOTHESIZED STRUCTURAL/PHYSICAL RISK FACTORS		
Housing type and age	Inadequate housing and overcrowding have been linked in many studies to poor mental health status and developmental delays	Bashir 2002; Myers et al. 1996
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Margai and Henry 2003
	Review study on literature over the past several decades suggested that linkages exist between numerous aspects of housing and mental health.	Evans et al. 2003
	Ethnicity, age, immigration, and poverty play important roles in home overcrowding	Myers et al. 1996
	Housing type moderates relationships between crowding and mental health in children; children living in multiple-family dwellings have stronger adverse reactions to overcrowding that those living in single-family or row houses	Evans et al. 2002

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Structure/construction/ condition	Review study: Housing quality characteristics were positively correlated with psychological well-being, including structural deficiencies, cockroach and rodent infestations, dampness, and mold	Evans et al. 2003
	Housing structural quality was significantly related to child's level of psychological distress and motivation	Evans et al. 2001a
	Children who face more cumulative risk (based on elements of physical housing quality and psychosocial factors) have greater psychological distress	Evans 2003b
	Neighborhood physical conditions (as indicated by boarded-up housing) may be related to certain causes of premature mortality	Cohen et al. 2003a
Electrical system		
Fire Related Factors		
Building Materials	*See "Lead" row under "Chemcial Risk Factors" below*	
HVAC		
Moisture	*See "Structure/construction/condition" row under "Hypothesized Structural/Physical Risk Factors" above*	Evans et al. 2003
	Nervous system effects, suppression of immune response, and hemorrhage in mucous membranes of intestinal and respiratory tracts may be associated with damp environments or exposures resulting from damp environments	NAS 2004
	Molds can produce mycotoxins under certain environmental conditions (e.g., in the presence of water-soaked cellulosic materials), some of which are known neurotoxins in certain exposure scenarios	Kelman et al. 2004; Burge and Amman 1999
	There is very little information in the literature on the potential toxic exposure associated with damp environments	Bornehag et al. 2004; NAS 2004
	Review study (through 2003): There is inadequate information to determine whether damp indoor environments or associated agents are related to neurological health outcomes	NAS 2004
Cleanliness		
Safety devices		
HYPOTHESIZED CHEMICAL RISK FACTORS		
Pesticides	Lead, mercury, polychlorinated biphenyls (PCBs), and several types of pesticides have been extensively researched in laboratory studies and found to cause catastrophic developmental effects at higher-dose exposures and a variety of neurodevelopmental problems at lower levels of exposure	Stein et al. 2002
	Human mother-infant cohorts accidentally exposed to high concentrations of PCB, dioxins, and pesticides provide evidence that certain chemical exposures can affect the developing nervous system and cause adverse cognitive and neurobehavioral effects later in life	NRC 1999
	Review study: House dust was identified as an important pathway of residential exposure via inhalation of suspended particles and ingestion; pesticide contaminants appeared to often exceed tolerable exposure concentrations	Butte and Heinzow 2002
	In-home interviews and inventories: Over 850 unique pesticide products currently being used by sample households; 97% had pesticides on the premises; 88% reported use of pesticides; no significant differences in urban vs. non-urban residential storage and use patterns	Adgate et al. 2000
	Per state and local waste pesticide collection and disposal programs: Large (but unquantified) amounts of pesticides, including banned pesticides, remain in storage in residential and agricultural settings and could pose a serious environmental and human health threat if released	Fitz and Andreasen 2002; EPA 2002c
	Studies conducted in last 10 years have documented the presence of numerous different pesticides in indoor air, carpet dust, and settled dust of home surfaces	Rudel et al. 2003
	Pesticides are present indoors at widely varying levels that, on a compound by compound basis, often do not appear to constitute an immediate health risk	Gordon et al. 1999; Nishioka et al. 1999; Roinestad et al. 1993; Simcox et al. 1995; Whitmore et al. 1994

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	There are two major unknowns in the determination of potential health outcomes: the health impacts and outcomes from chronic pesticide exposures and the cumulative effects of exposures to multiple compounds	EPA 2000b; Weiss 2000
	727,036 cases of nonpharmaceutical pediatric (<6 years of age) poisonings were documented in the U.S. in 2002; 92% of all exposures occurred in the home	Watson et al. 2003
	Given the toxicity of all insecticides toward some nervous system component, it is believed that children are particularly at risk because complete development of the nervous system does not occur until late in childhood	Hall et al. 1997
	Low-dose, chronic pesticide exposure may negatively impact the nervous system; animal data and in-vitro work suggest that chronic pesticide exposures might be tied to learning and behavioral problems	Chanda and Pope 1996; Rice et al. 2000
	Children exposed to an illegally applied organophosphate pesticide experienced behavioral/motor skill problems and difficulty with tasks involving attention and short-term memory; inconsistent results prevented authors from conclusively attributing any neurobehavioral health effects to the pesticide studied	Ruckart et al. 2004
	Review study: Despite the volume of studies on chronic health outcomes associated with pesticide use, very few conclusions can be made	Colosio et al. 2003
	Organophosphates inhibit nerve transmission, interfere in acquisition and development of new brain cells, and inhibit DNA synthesis; these functions are critical to proper neurological development	Whitney et al. 1995; Dam et al. 1998; Li and Casida 1998; Rice and Barone 2000; Weiss 2000
	Even with full implementation of pesticide use precautions, residues can remain in a home for years after use, and chronic exposures may occur	Whitmore et al. 1994
	Roughly 90% of homes in the U.S. use chemicals to control pests	Landrigan et al. 1999
	Laboratory studies on oral toxicities of Type I and II pyrethroids in rats, together with data on toxicities of diazinon and chlorpyrifos, indicate that many pyrethroids approach the toxicities of the organophosphates	Kamrin 1997; Miyamoto 1976; Elliott 1977; Worthing 1983
	Indoor pesticide persistence is further exacerbated by the presence of household materials such as carpets, upholstered furniture, and draperies that act as sorbents or reservoirs resulting in subsequent slow release of pesticides over time	Cohen Hubal et al. 2000; Pang et al. 2002
	Indoor air and house dust in structures previously treated with persistent organochlorines can have residual pesticide levels as much as 10-100 times higher than in outdoor air and surface soil	Lewis et al. 1988; Whitmore et al. 1994; EPA 2000c; Wilson et al. 2003
	Carpet fibers and binder are the predominant reservoirs for pesticide residue; carpet padding retains a small amount; very little residue found on carpet surface, suggesting that pesticide residues in carpet would not be easily dislodged	Fortune et al. 2000
	Chlorpyrifos residue continued to accumulate on and in toys and other sorbent surfaces for two weeks following application	Gurunathan et al. 1998
	Pesticide residues were easily redistributed from application areas to surfaces accessible to children (e.g., toys) following outdoor and indoor chlorpyrifos application; outdoor pesticides can be tracked indoors or penetrate indoor area through spray drift	Lewis et al. 2001
	NHEXAS: Inhalation of indoor air accounted for 84.7% of aggregate daily exposure to chlorpyrifos; short-term air measurements of chlorpyrifos were highly variable over time; chlorpyrifos concentrations in indoor air and carpet dust were significantly correlated; carpet levels were less variable over time	Pang et al. 2002
	Tracking may be a more important factor than spray drift in the distribution of lawn pesticides indoors	Nishioka et al. 1999
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Lu et al. 2000
	Pesticides are of particular concern in low-income, inner-city areas, where conditions favor pest infestation; considerable exposure to indoor pesticides was found within a cohort of multi-ethnic, urban women	Berkowitz et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	Strong associations were observed between dilapidated housing and pesticide exposures; a high degree of correlation was found between maternal pesticide levels and levels found in cord blood samples	Whyatt et al. 2002
Other organic chemicals	There is little information available to evaluate the potential for industrial chemicals to cause neurodevelopmental damage, even where population wide exposures are documented	Weiss and Landrigan 2000; Schettler 2001; Stein et al. 2002; Goldman and Koduru 2000
	No screening level developmental toxicity information is available for about 78% of all HPVs, or over 45% of HPVs commonly found in consumer products	Goldman and Koduru 2000
	Laboratory studies have established that PCBs are neurotoxins in animals exposed pre- and post-natally, even at low doses	ATSDR 2000
	Although uses of PCBs in building materials have been discontinued for years, it is believed that these materials may still be present in some older structures (e.g., plaster and caulk)	Herrick et al. 2004; Andersson et al. 2004; Wilkins et al. 2002
	Brominated flame retardants (BFRs) are ubiquitous in environmental media, wildlife, and in humans; though animal studies indicate that BFRs can cause nervous system disruption and other effects, data on human exposures and health effects is very limited	ATSDR 2002
	Significant amounts of dioxin compounds are produced as a contaminant of the wood preservative pentachlorophenol (PCP) and are tied up in PCP-treated products	EPA 2000d; ATSDR 1998
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Dahlgren et al. 2003b
Combustion by-products	CO residential poisoning discussed in Injury section	
Lead	*See "Pesticides" row under "Hypothesized Chemical Risk Factors" above*	Stein et al. 2002
	Moderate childhood lead poisoning can cause permanent neurological effects; at higher exposure levels, potential effects include anemia, kidney injury, nerve injury, brain dysfunction, seizures, coma, and death; prenatal exposure can result in premature births, low birth weight, decreased mental ability in the infant, learning difficulties, and reduced growth in young children	ATSDR 1999a
	The effects of prenatal lead exposure may extend into later life and must be further investigated as risk factors for adult psychiatric diseases	Opler et al. 2004
	Evidence suggests that deficits in cognitive and academic skills associated with lead exposure have no lower threshold; the magnitude of the effect and shape of the dose response relationship at blood lead levels <10 µg/dL are still uncertain.	Lanphear et al. 2000; Canfield et al. 2003; Bellinger et al. 2003
	Children at highest risk for lead exposure fall into two major groups: impoverished children living in older, poorly maintained rental housing and more affluent children living in older housing undergoing renovation; even subtle deterioration of interior lead-based paint can create a significant dust hazard	Lanphear 2003
	National Survey of Lead and Allergens in Housing: Approximately 40% of housing units in the U.S. contain lead-based paint; 25% of the nation's housing stock have one or more significant lead-based paint hazards; 1.2 million housing units pose the highest risk of lead poisoning because they housed low income families with children less than six years	Jacobs et al. 2002
	Analysis of lead concentration data from exterior entry, perimeter soil, street dust, interior dust wipe, and paint lead samples showed a wide range of exterior dust and soil lead levels	Clark et al. 2004
	Almost two-thirds of the lead in house dust appeared to be derived from outdoor sources	Adgate et al. 1998
	Based on a study simulating wall enclosures, under less-than-extreme conditions, dust would have to be released for years without cleaning to yield a hazard	Harney et al. 2000
	Children appear to receive the highest dust lead exposures during the summer, with the seasonality of blood lead levels related to the seasonal distributions of dust lead in the home	Yiin et al. 2000
	See "SES Mediators" row under "Hypothesized Behavioral & SES Risk Factors" below	Lanphear et al. 1998a
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Rabito et al. 2003
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Margai and Henry 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Other inorganic chemicals	Mercury compounds are among the most potent developmental neurotoxicants and can permanently damage the brain, kidneys, and developing fetus at high levels of exposure	ATSDR 1999b
	Methylmercury exposure levels that do not result in symptoms in pregnant experimental animals adversely affect the offspring's development; studies suggest this may also occur in humans	Meyers and Davidson 2000; Mahaffey 2000
	Questions have been raised about a potential link between mercury exposure and autism spectrum disorders/other adverse neurodevelopmental outcomes; human exposures typically occur at low to moderate doses, however, and data on neurotoxic health effects at low doses are relatively limited	Davidson et al. 2004
	Low level exposures to methylmercury in utero can have adverse effects on neurobehavioral development	NRC 2000
	Review study: Potential sources of mercury include: elemental mercury vapor exposure through accidents (e.g., thermometer breakage), occupational and ritualistic use of elemental mercury (e.g., folk medicine practices, especially among inner-city immigrant populations);, inorganic mercury exposure through the use of topical mercury-based skin creams and in infant teething powders; and metallic mercury in dental amalgams	Counter and Buchanan 2004
	Mercury is potentially present in consumer products such as control components in household appliances, automobile components, old paint, cleaners, computers, electric equipment, lamps, personal care products, and recreational products	Draft Wisconsin Mercury Sourcebook 2004; IMERC 2004; Kuiken 2002
	For most people, the major exposure to arsenic comes from food, although localized cases of chronic arsenic poisoning due to natural contamination of ground water and wells have also been documented	Ahmad et al. 2001; Calderon et al. 2004
	Components of CCA may leach from treated wood surfaces into surrounding soil, elevating concentrations of arsenic, chromium, or copper; elevated concentrations of all CCA components were found close to and under structures, with new structures exhibiting higher concentrations in surface soils than older structures; variations in soil concentrations were also apparent locally	Chirenje et al. 2003
	Arsenic doses in amounts of tens of micrograms per day may be incurred by children having realistic levels of exposure to CCA-treated decks and playground structures.	Hemond and Solo-Gabriele 2004
	A controlled garden experiment using CCA-treated wood found that arsenic concentrations in crops remained well below the recommended limit in foods	Rahman et al. 2004
	18 of 22 samples collected from construction and demolition debris processing facilities leached arsenic at concentrations exceeding Florida's Groundwater Clean Up Target Level; researchers estimated that mulch containing <0.1% CCA-treated wood would likely exceed Florida's residential clean soil guideline	Townsend et al. 2003
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Meyer et al. 1999
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" below	Belluck et al. 2003; ATSDR 2000; Wolz et al. 2003
	Arsenic contamination due to past pesticide application (e.g., arsenical crabgrass killer and insecticide (PAX)) has been found in current residential areas	Folkes et al. 2001
Also see "Ambient air pollution" and "Traffic" under External Factors Affecting Housing		
HYPOTHESIZED BIOLOGICAL RISK FACTORS		
Multiple allergens		
Dust mites		
Cockroaches	*See "Structure/construction/condition" row under "Hypothesized Structural/Physical Risk Factors" above*.	Evans et al. 2003
Other insects (ticks, fleas, mosquitoes)		
Mice		
Rats		
Other rodents	*See "Structure/construction/condition" row under "Hypothesized Structural/Physical Risk Factors" above*	Evans et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Molds	The majority of the data regarding neurological effects of mold exposure is from animal studies or human poisoning cases due to the ingestion of mycotoxin-contaminated food	Bennett and Klich 2003
	Sufficient data from animal models and human epidemiological data indicates that mycotoxins pose an important human health risk, there is inadequate information to determine whether molds or associated agents are related to neuropsychiatric health outcomes in residential exposure scenarios	NAS 2004
	Current scientific evidence does not support the proposition that human health has been adversely affected by inhaled mycotoxins in the home, school, or office environment	Hardin et al. 2003
	Current evidence supports relationships between excessive moisture, mold growth, and increased prevalence of irritation/allergy/infection symptoms, specific human toxicities due to inhaled fungal toxins were not scientifically established	Fung and Hughson 2003
	A model of the maximum possible dose of mycotoxins that could be inhaled in 24 hours indicated that none of the maximum doses were sufficiently high to cause any adverse effects	Kelman et al. 2004
	Preliminary evidence suggests that indoor mold exposures were associated with neurobehavioral and pulmonary impairments that likely resulted from the presence of mycotoxins	Kilburn 2003
	Results of study of neurophysiological effects in 10 children who attended a health center because of chronic indoor toxic mold exposure suggested significant neurological deficits in all the patients compared to controls	Anyanwu et al. 2003
Pets		
Bacteria, endotoxins, microbial VOCs (mVOCs)		
Other triggers (e.g., viral agents, parasites)		
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS		
Location	*See "Lead" row under "Chemcial Risk Factors" above*	Lanphear et al. 1998a
	Results found no differences between children residing in New Orleans housing developments and children in non-development housing.	Rabito et al. 2003
	See "Other inorganic chemicals" row under "Chemical Risk Factors" above	Chirenje et al. 2003
	Area of residence was the most significant factor associated with arsenic levels in interior dust fall in a German study; loading rates were most elevated in inner city areas, which are in closest proximity to the smelters and tailings piles	Meyer et al. 1999
	Past use in the U.S. has left many current and former agricultural sites with soil arsenic concentrations; homes near land used for apple/pear production between 1905 and 1947 had significantly higher soil arsenic than other homes; 36% had soil or dust arsenic levels above the minimum risk level estimated by ATSDR	Belluck et al. 2003; ATSDR 2000; Wolz et al. 2003
	Adverse health effects, including cancer, respiratory, skin, neurological health problems, and neurophysiologic abnormalities among adults, appeared to be more prevalent in long-term residents near a PCP wood treatment plant	Dahlgren et al. 2003b
	Areas at high risk for learning disabilities were strongly associated with historically significant sources of lead toxicity and air pollution facilities, the presence of multiple/subdivided housing units, poverty, higher percentage of residents on public assistance and lower adult educational attainment	Margai and Henry 2003
	Rates of impaired development (and numerous other adverse health outcomes) are disproportionately high in certain underserved, urban, minority populations	Perera et al. 2002
	Rural populations may also be at increased risk for certain exposures such as pesticides	Eskenazi et al. 1999; Wolz et al. 2003
	Children living in agricultural areas may be exposed to higher pesticide levels than other children because of pesticides tracked into their homes by household members, by pesticide drift, or by playing in nearby fields	Eskenazi et al. 1999
	Pesticide exposure levels of children whose parents use agricultural chemicals or who live near farmland treated with pesticides were found to be significantly higher than those of other children living in the same community	Lu et al. 2000

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	Because pesticides are used extensively in urban schools, homes, and day care centers for urban vermin control, pesticide use in inner city areas is a key component of neurotoxic risk faced by children in theses areas	Landrigan et al. 1999
	Effects of neighborhood location and past uses have also been observed with regard to exposure to potentially neurotoxic chemicals	Wolz et al. 2003; Folkes et al. 2001
Zoning/building codes	Noxious land uses tend to be concentrated in poor and minority areas	Maantay 2001
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" above	Meyer et al. 1999
Ambient air pollution	Young, inner-city New York students were exposed to a wide range of toxic air pollutants, such as volatile organic compounds (VOCs), aldehydes, particulate matter <2.5 micrometers, black carbon, and particle-associated trace elements	Kinney et al. 2002
	See "Location" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" above	Margai and Henry 2003
Traffic		
Noise	Much of the noise-related research to date shows inconsistencies between laboratory and occupational studies and community field studies, with effects being much less pronounced in field studies where adaptation occurs	Stansfeld and Matheson 2003
	Children in high noise areas had higher levels of annoyance and impaired reading comprehension; at follow-up, chronic aircraft noise exposure was still associated with higher levels of annoyance/perceived stress, poorer reading comprehension and sustained attention, suggesting that adaptation was not occurring	Haines et al. 2001a, 2001b
	Chronically increased stress hormone levels were reported in adult women exposed to traffic noise	Babish et al. 2001
	Sleep difficulties were reported in adults living within the flight pattern of a major airport	Bronzaft et al. 1998
	Areas of greater affluence had a significantly greater proportion of highly annoyed persons due to aircraft noise compared to more disadvantaged areas	Whitfield 2003
	Children in areas with higher ambient noise had modestly elevated resting blood pressures and overnight urinary cortisol, elevated heart rate reactivity, and rated themselves higher in perceived stress symptoms; girls, but not boys, also exhibited diminished motivation in a standardized behavioral test	Evans et al. 2001b
	Exposure to ambient noise was associated with poorer classroom behavior and small decrements in children's mental health; correlation between mental health and ambient noise was only significant in children with additional risks	Lercher et al. 2002
Crime rates, violence, neighborhood safety	Residents of disadvantaged neighborhoods generally had worse health than residents in more advantaged neighborhoods, with the effect mediated by fear of perceived neighborhood disorder (based on measures of crime)	Ross and Mirowsky 2001
	Youth in low SES neighborhoods had lower mental health ratings than those in high SES neighborhoods due to perceived dangers in their communities and to a lesser extent because of a perceived lack of social cohesion	Aneshensel and Sucoff 1996
	Collective efficacy, defined as social cohesion among neighbors and their willingness to intervene on behalf of the common good, is linked to reduced community violence; the association between violence and disadvantaged, instable neighborhoods is strongly mediated by collective efficacy	Sampson et al. 1997
Recreational facilities, playground equipment		
Pedestrian and bicycle access		
Water hazards		
HYPOTHESIZED BEHAVIORAL & SES RISK FACTORS		
SES mediators	Community level variables associated with an increased risk of elevated BLL in children included: lower housing value, older housing, higher population density, higher poverty rates, lower % of high school graduates, and lower rates of owner-occupied housing; majority of those with elevated BLL lived in the city	Lanphear et al. 1998a
	School district community contextual variables (including community education level, % of children in poverty, etc.) accounted for up to 63% of the variance in adolescent academic achievement	Baker and Davis 2001

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	Moving to low-poverty neighborhoods had positive effects on 11-18-year-old boys' achievement scores compared with those of their peers in high-poverty neighborhoods	Leventhal and Brooks-Gunn 2004
	Parents who moved to lower poverty neighborhoods reported significantly less distress than those remaining in higher poverty neighborhoods; boys who moved to less poor neighborhoods reported significantly fewer dependency and anxious/depressive problems than boys who stayed in public housing	Leventhal and Brooks-Gunn 2003
	Higher rates of major depression and substance abuse were found in individuals from disadvantaged neighborhoods; higher rates of schizophrenia, major depression, and substance abuse were associated with neighborhood residential mobility	Silver et al. 2002
	Personal income, community socioeconomic condition, and perceived social support from the neighborhood were significantly associated with a person's mental health status	Yang 2000
	It is difficult to differentiate whether the poorer health observed in disadvantaged neighborhoods is primarily a function of lower SES, or whether there are additional factors in disadvantaged neighborhoods that contribute to the effect	Ellen et al. 2001
	See "Crime rates, violence, neighborhood safety" row under "Hypothesized External Factors Affecting Housing & Neighborhood Risk Factors" above	Ross and Mirowsky 2001
	Residential neighborhood problems function as sources of chronic stress that may increase risk of poor health	Steptoe and Feldman 2001
	Non-income community level factors mediate the effect of socioeconomic status on premature mortality	Cohen et al. 2003b
	The effects of poverty or income on health are mediated by exposure to multiple environmental risk factors	Evans and Kantrowitz 2002
Other behavioral factors		

As shown in Table 3.2-1, the bulk of literature regarding neurological and psychiatric outcomes uncovered during this review was focused on select chemical exposures in residential environments, primarily lead and pesticides. Health effects related to mercury and polychlorinated biphenyl exposures, in children as well as pregnant women, have also been the subject of numerous studies, although only a small portion of this literature has tied exposures to housing or neighborhood factors. Several other chemical exposures with the potential to occur in residential environments, such as those associated with wood preservatives, were also reflected in the literature. A modest body of research was also found to exist on the effects of housing quality (e.g., condition, crowding, etc) on mental health, including a review study and development of a housing quality index specifically geared to assess quality factors that might affect psychological health.

The following sections detail the literature found on specific housing and neighborhood related risk factors for neurodevelopmental, neurobehavioral, and mental health outcomes.

3.2.3 Structural/Physical Attributes of Housing/Neighborhoods Associated with Neurobehavioral Development, Developmental Disabilities and Psychiatric Outcomes

Numerous types of physical housing attributes have been associated in the literature with neurological outcomes. These include associations between mental health and housing type/crowding, housing quality, and cleanliness. The types and condition of certain building materials used in and around homes have the potential to expose children to a variety of chemicals, some of them neurotoxins. These materials, such as lead-based paint (i.e., chipping

paint), wood preservatives (e.g., PCP, CCA), and solvents are discussed specifically in Section 3.2.4 on chemical exposures. In addition, some literature was found that examined associations between damp indoor environments and nervous system effects; this is discussed briefly below (see "Moisture") and in more detail in Section 3.2.5 on mold/biological exposures.

Housing Type and Crowding. Inadequate housing and overcrowding have been linked in many studies to poor mental health status and developmental delays (Bashir, 2002; Myers et al., 1996). For example, in a geo-statistical study of childhood disabilities, Margai and Henry (2003) identified a positive association between childhood learning disabilities and multiple/subdivided housing units.

In a review study, Evans et al. (2003) examined a substantial body of research conducted over the past several decades on mental health as related to housing characteristics. Housing factors examined included housing type (e.g., single-family detached versus multiple unit dwellings; low-rise versus high-rise buildings), and floor level of dwelling. Results of the review suggested that linkages exist between numerous aspects of housing and mental health. For example, in general, people living in high-rise buildings appeared to have more mental health problems than those living in low-rises or single-family detached homes. Several studies also found that residents of higher floor levels in high-rise buildings suffered from poorer mental health. Explanations for these associations suggested by the reviewers include social isolation, lack of access to play spaces for children, and anxiety about falls and accidents. The authors of the review, note, however, that in some of the studies reviewed there were weaknesses in study designs particularly with regard to controlling for socioeconomic status. Nonetheless, they conclude that sufficient evidence does exist in the body or housing and mental health literature as a whole to support a linkage between housing and psychological health, particularly for low-income families with young children.

Regarding overcrowding, researchers suggest that one of the major underlying psychological processes that appears to account for some of the negative effects of crowding is loss of control over interpersonal interaction (i.e., too much unwanted social interaction) (Evans et al., 2002). Determining the factors that lead to overcrowding, however, has proved complex – proposed explanations have included restrictions on housing availability, housing affordability, low incomes, racial and ethnic diversity/immigrant concentrations, and consumer preferences (Myers et al., 1996).

Myers et al. (1996) conducted an analysis of national housing data from the 1990 census to measure and describe the growing prevalence of residential overcrowding, as well as local factors that explain the marked variation in levels of residential crowding between locales, and between ethnic and racial groups. Overcrowding was assessed in the study in terms of the per room density of people in their housing, or persons per room (PPR). It is important to note that the PPR overcrowding standards are relatively subjective and have changed over time. The conventional standard applied by local and federal governments in 1940 was > 2.00 PPR, but it was lowered to > 1.50 PPR by 1950, and down to > 1.00 PPR by 1960. The Myers et al. study focused on the "more than 1 PPR" standard, in use since 1960. Results of the analysis suggested that ethnicity, age, immigration, and poverty play important roles in home overcrowding. Housing market conditions were also a factor, but appeared much less important. Findings indicated that overcrowding is not distributed equally among households in the U.S., but that

recent immigrants, Asians, Hispanics, and lower-income households are most at risk of being overcrowded. Relative to home owners, renters were also more likely to suffer from overcrowding. The highest rates of overcrowding were found among recent immigrants who arrived in the U.S. during the 1980s and 1970s (this was not the case among those who arrived before 1970). Differences in the rates of overcrowding between the lowest and highest income categories was also pronounced, but overcrowding rates did not appear to drop substantially until households exceed 200 percent of the poverty level, or until relative income passed the median level. Finally, looking at state-to-state differences, California and Hawaii (two states with notoriously expensive housing) had rates of overcrowding that far exceeded the others states.

Evans et al. (2002) investigated the relationships between residential crowding, housing type, and mental health in a study of 1,236 Austrian children in third and fourth grade living in small towns and agricultural areas. In the study, measures of residential density (people per room) and housing type (multiple family unit, row house, single family detached) were compared to two standardized scales of psychological health (KINDL scales for emotional well-being and functional impairment) and teacher ratings of classroom behavior. Results of the study indicated that housing type moderated the relationships between crowding and mental health in children, with children living in multiple-family dwellings having stronger adverse reactions to overcrowding that those living in single-family or row houses. The authors note that although researchers have tended to focus on the direct effects of crowding, these results emphasize the fact that housing design variables, similar to individual-level variables (e.g., SES), can function as moderators of psychosocial processes.

Housing Condition and Cleanliness. Several studies conducted by researchers at Cornell University were identified in the course of this literature search that examined relationships between housing quality and mental health, including two that attempted to develop and apply a housing quality index to more adequately reflect the multidimensional physical qualities of housing rather than focusing solely on individual housing attributes such as crowding or noise (Evans et al., 2001a; Evans et al., 2000).

As discussed above, Evans et al. (2003) conducted a review study to examine research conducted over the past several decades on mental health as related to housing characteristics. Numerous housing quality characteristics were positively correlated in the review with psychological distress, including factors such as structural deficiencies, cockroach and rodent infestations, dampness, and mold. The reviewers suggest that housing quality may specifically affect mental health by creating identity and self-esteem issues, anxiety about housing hazards (especially where children are in the home), worry and lack of control over maintenance and management practices, and fear of crime in unsecured housing.

To examine the potential link between housing quality and mental health, Evans et al. (2000) attempted to develop a valid and reliable, observer-based instrument designed to assess physical housing quality specifically in relation to psychological outcomes. The 88 attributes of housing and neighborhood quality included in the index (in areas focusing on child resources, cleanliness/clutter, indoor climatic conditions, privacy, hazards, and structural quality) were assessed by trained raters to avoid problems associated with residents' self-reports of both housing quality and health outcomes. Along with housing quality, psychological distress was

measured in a cross-sectional sample of rural women of varied SES (n=207) and a longitudinal sample (before and after moving to better quality housing) of urban women (n=31) using the Demoralization Index of the Psychiatric Epidemiology Research Instrument (PERI). Analyses of internal consistency, agreement across observers, and factor intercorrelation indicated that the housing quality index developed was a reliable and valid instrument. Further analysis of data using the newly developed instrument indicated that improved housing quality did benefit mental health in these cohorts of women. In a follow-on study that employed the observer-based Housing Index developed previously (Evans et al., 2000) to measure housing quality, Evans et al. (2001a) assessed 277 children in grades three through five regarding potential relationships between poor quality housing and psychological distress and behavioral symptoms. Children included in the study were ethnically/racially diverse, and came from families ranging from below the poverty level up to four times the poverty level. The families resided in both rural and urban communities, and nearly all lived in single-family detached homes or in apartments located in two- or three-family houses. None of the participants resided in large, multi-story housing units. A standardized index of children's psychological health, the Rutter Children's Behavior Questionnaire, was used to assess psychological health, and a task persistence test (to indicate learned helplessness, an integral component of human motivation) was used as an index of behavioral status. Controlling for SES, results of comparisons of the housing quality index and mental health outcomes showed that housing quality (e.g., safety of stairs, holes in wall or ceilings, number of times furnace has broken down, clutter in kitchen) was significantly related to the child's level of psychological distress and motivation (with increased housing quality being associated with fewer behavioral problems and higher levels of persistence on the unsolvable puzzle). These results led the authors to conclude that children living in lower-quality housing, independent of household income, have more symptoms of psychological distress and less task persistence than children living in better quality housing.

In a study of 339 rural children from New York state (about half of them below the poverty line), Evans (2003b) attempted to assess risk of psychological distress based on a model of cumulative risk that incorporated elements of physical housing quality (e.g., crowding, noise structural quality, clutter and cleanliness, hazards, indoor climate), as well as psychosocial factors (e.g., child separation, turmoil, violence). Results of the study suggested that children who face more cumulative risk have greater psychological distress, emphasizing the importance of looking at the residential environmental holistically when attempting to assess children's risk.

Moisture. Although the majority of health effects researched in association with indoor moisture problems and resulting exposures (e.g., to molds or bacteria) have been focused on respiratory health outcomes, some studies report that other effects – including nervous system effects, suppression of the immune response, and hemorrhage in the mucous membranes of the intestinal and respiratory tracts – may be associated with damp environments or exposures resulting from damp environments (NAS, 2004). Under the appropriate environmental and competitive conditions (e.g., in the presence of water-soaked cellulosic materials) molds can produce mycotoxins (Burge and Amman, 1999), some of which are known neurotoxins in certain exposure scenarios (Kelman et al., 2004). Excessive moisture indoors may also encourage the growth of bacteria that produce substances (e.g., endotoxins) which could have toxic or inflammatory effects. In addition to mold and bacteria related exposures occurring under damp conditions, water damage could promote the degradation of building materials, furniture, etc., which may in turn result in toxic organic chemical releases; however, there is very little

information in the literature on this potential toxic exposure associated with damp environments (NAS, 2004; Bornehag et al., 2004).

In an assessment of the whole body of literature on the topic, however, health effects research examined by the IOM (through 2003) indicated that there was inadequate or insufficient information to determine whether damp indoor environments or the agents associated with them are related to neurological health outcomes (NAS, 2004). In addition, the IOM noted that the relationship between dampness or specific dampness-related agents and health effects is sometimes unclear and in many cases indirect (NAS, 2004).

Specific literature with regard to moisture related mold and endotoxin exposures and potential neurological outcomes is discussed in Section 3.2.5 below on biological exposures. Additional discussion of causes and exposures associated with moisture problems in homes is included in Section 3.4.3 of this report on asthma and other respiratory outcomes.

3.2.4 Chemical Attributes of Housing/Neighborhoods Associated with Neurobehavioral Development, Developmental Disabilities and Psychiatric Outcomes

Numerous types of toxic chemical exposures, many of them commonly encountered in household and residential environments, are capable of causing neurodevelopmental disabilities in children. For example, lead, mercury, polychlorinated biphenyls (PCBs), and several types of pesticides have been extensively researched in laboratory studies and found to cause catastrophic developmental effects at higher-dose exposures, as well as a variety of neurodevelopmental problems (e.g., impairments in attention, memory, learning, social behavior) at lower levels of exposure comparable to those currently experienced by significant portions of the general human population (Stein et al., 2002). Studies of human mother-infant cohorts accidentally exposed to high concentrations of PCB, dioxins, and pesticides also provide evidence that certain chemical exposures can affect the developing nervous system and cause adverse cognitive and neurobehavioral effects later in life (NRC, 1999). However, for many of these chemicals (with the clear exception of lead), investigations of pathways of potential exposure in residential environments have been limited. Furthermore, for the overwhelming majority of industrial chemicals in widespread use in the U.S. today, there is little information available to evaluate the potential for these chemicals to cause neurodevelopmental damage, even where population-wide exposures are documented (Weiss and Landrigan, 2000; Schettler, 2001; Stein et al., 2002; Goldman and Koduru, 2000).

Regarding residential exposure pathways to chemical contaminants, Butte and Heinzow (2002) conducted a review of the literature presenting data on the occurrence of organic and inorganic contaminants in house dust. Many of the studies reviewed identified house dust as an important pathway of residential exposure, both through inhalation of suspended particles and via ingestion (especially for small children). Contaminants in house dust reported in the literature reviewed by Butte and Heinzow (2002) included PCBs, polycyclic aromatic hydrocarbons (PAH), pesticides, plasticizers (phthalates, phenols), flame retardants, as well as other organic xenobiotics and inorganic constituents such as lead. By comparing reported contaminant levels (at an assumed daily intake of 100 mg house dust) to the chronic oral reference doses (RfD), several of the pesticide contaminants (including DDT, diazinon, but especially chlorpyrifos) appeared to often be at levels exceeding tolerable exposure concentrations.

In addition to the types of chemical exposure mentioned above, prenatal exposure to tobacco constituents via environmental tobacco smoke (ETS) is also a serious and common environmental hazard for children. The links between maternal smoking and low birth weight, decreased lung growth, infections, and childhood asthma, are well established in the literature (DiFranza et al., 2004). In addition, associations have been reported between children's prenatal exposure to ETS and behavioral problems and neurocognitive decrements (DiFranza et al., 2004). However, because smoking may be fundamentally considered a behavioral issue, it is not addressed in the current review, but will be an important covariate in most analyses relating indoor exposures to health effects.

Lead. Dramatic reductions in children's blood lead levels (BLLs) have been observed over the past 15 years, in large part due to the phase-out of lead in gasoline under the Clean Air Act, passage of the 1971 Lead-based Paint Poisoning Prevention Act, and the banning of lead-based paint. Nonetheless, children continue to be exposed to lead hazards through residential sources such as lead-based paint chips (e.g., young children eating paint chips from older deteriorated housing), chewing on objects painted with lead-based paint (e.g., cribs), or swallowing house dust or soil that contains lead.

Even moderate childhood lead poisoning can cause permanent neurological effects. BLLs greater than or equal to 10 µg/dL have been linked in many studies to various neurodevelopmental effects, especially learning disabilities and behavior problems, and increasing blood-lead levels have been highly correlated with decreased performance on standardized intelligence tests (i.e., lower I.Q. test scores) (ATSDR, 1999a). According to data from the Centers for Disease Control and Prevention (CDC) National Health and Nutrition Examination Survey (NHANES) data, 2.2% of children (i.e., about 434,000) aged 1-5 years had BLLs greater than or equal to the CDC recommended limit of 10 µg/dL in 1999-2000 (CDC, 2003). Higher prevalence of elevated BLLs were also observed in urban children, those in lower socioeconomic groups, immigrants, and refugees (CDC, 2003).

At higher levels of lead exposure, more pronounced health effects can occur, including anemia, kidney injury, nerve injury, brain dysfunction, seizures, coma, and even death (ATSDR, 1999a). Acute injuries to children as a result of lead exposure are discussed in Section 3.3.4 of this report.

Prenatal exposure to lead can also result in adverse health effects including premature births, low birth weight, decreased mental ability in the infant, learning difficulties, and reduced growth in young children (ATSDR, 1999a). As discussed previously in Section 3.1.3 on maternal exposures, Opler et al. (2004) tested the hypothesis that environmental lead exposure during prenatal development may be associated with schizophrenia using archived serum samples from a cohort of live births in Oakland, California between 1959 and 1966. Serum analyses showed elevated levels of a biologic marker of lead exposure (delta-ALA) in numerous samples, with an odds ratio for schizophrenia associated with the highest category (equivalent to a blood lead level greater than or equal to 15 µg/dL) of 2.43 (95% CI, 0.99-5.96; $p = 0.051$). The authors suggest that the effects of prenatal lead exposure may extend into later life and must be further investigated as risk factors for adult psychiatric diseases.

As blood lead levels have dropped over the years, recent analyses have also examined the relationship between relatively low blood lead concentrations (<10 µg/dL) and cognitive functioning in a representative samples of U.S. children and adolescents, and have found evidence that suggests that deficits in cognitive and academic skills associated with lead exposure have no threshold (Lanphear et al., 2000; Canfield et al., 2003; Bellinger et al, 2003). However, the magnitude of the effect and the shape of the dose response relationship at blood lead levels less than 10 µg/dL are still uncertain.

Beyond characterizing health effects, volumes of research have resulted in well-established and validated standards for various residential exposures (e.g., dust, soil), as well as assessment and abatement procedures (EPA, 1998). For example, the U.S. Environmental Protection Agency has identified hazardous levels of lead in house dust for floors and window sills, and bare residential soil (for play areas and in the rest of the yard) (EPA, 2001a).

While children under the age of six historically have been considered at risk for lead poisoning, perhaps the greatest risk and most severe injury occurs in children under the age of two because these are critical years in the development of the child and because young children engage in crawling and mouthing behaviors (e.g., hand-to-mouth activities) that provide a higher exposure to lead-based paint dust and paint chips (EPA, 1998). Many of the highest risk children fall into two major risk groups: impoverished children who live in older, poorly maintained rental housing (especially those who live in the northeastern and Midwestern regions of the United States) and more affluent children who live in older housing undergoing renovation (Lanphear, 2003). Current research shows that even subtle deterioration of largely intact lead-based paint on interior building components can create a significant hazard in household dust.

Based on results from the National Survey of Lead and Allergens in Housing (Jacobs et al., 2002), it is estimated that approximately 40 percent of housing units (38 million) in the United States contain lead-based paint. It is further estimated that 25 percent of the nation's housing stock (24 million housing units) have one or more significant lead-based paint hazards (i.e., deteriorated lead-based paint, lead-contaminated dust, or lead-contaminated soil). Overall, 1.2 million housing units represented those posing the highest risk of lead poisoning because they housed low-income families with children less than six years of age (Jacobs et al., 2002).

Numerous investigations of housing-level characteristics and lead concentrations and distributions in houses, as well as children's blood lead levels in some cases, were identified in this literature search. These studies looked at factors such as relationships between outside and inside lead dust concentrations, wall characteristics, and seasonal variation.

Clark et al. (2004) conducted a study of 541 homes in 12 state and local areas to investigate the relationships between exterior dust/soil lead and interior dust lead. Analysis of lead concentration data from exterior entry, perimeter soil, street dust, interior dust wipe, and paint lead samples showed a wide range of exterior dust and soil lead levels. Exterior entry dust lead was influenced by paint lead, and statistical modeling suggested transport of lead from exterior entry dust lead to interior entryway floors, other interior floors, and windowsills. In addition, geometric mean exterior entry dust lead concentrations were almost four times as high as street dust lead concentrations, suggesting that lead dust near housing was often a source of street dust

lead. Homes that had exterior soil treatments had lower post-intervention exterior entry, interior entry floor, windowsill, and other floor dust loading levels.

In a chemical mass balance source apportionment of lead in residential environments, Adgate et al. (1998) found that almost 50% of household lead dust came from street dust and soil, and 33% and 17% came from lead based paint and airborne lead particles, respectively. Thus, almost two-thirds of the lead in house dust appeared to be derived from outdoor sources.

In a laboratory study simulating potential wall enclosure failure, Harney et al. (2000) investigated the potential release of aerosolized leaded dust from inside wall spaces into rooms through gaps and cracks in the enclosure, with a focus on the effects of airflow and mechanical disturbances. Results of the experiment showed that dust was released primarily from the floor area immediately adjacent to the simulated enclosure gap, although significant releases occurred only under conditions of very high air flow and with large mechanical disturbances. The authors of the study concluded that under less-than-extreme conditions in homes abated using well enclosures, dust would have to be released for years without cleaning to yield a hazard.

Yiin et al. (2000) conducted a study to examine potential seasonal effects on residential dust lead concentrations, and any relationships to blood lead in preschool children. Analyses of blood and house dust samples collected from 135 children in 67 New Jersey homes between June 1992 and September 1995 indicated that children appear to receive the highest dust lead exposures during the summer, with the seasonality of blood lead levels related to the seasonal distributions of dust lead in the home. In addition, the authors suggest that at least some of the summer peaks (June, July, August) in blood lead levels is likely due to children's seasonal activity patterns, i.e., children are likely to have increased exposure to lead in street dust and soil during longer outdoor play periods in summer. Another interesting finding of the study related to trends for carpet dust and lead loadings; carpets and rugs, which are known reservoirs for dust, had higher dust lead loading in cool and cold months than in hot months. The authors hypothesized that the cool and cold months include periods of snow and wet outdoor conditions that promote the carrying of mud or soil adhered to shoes or boots into houses. Therefore, during the cool and cold periods, carpet dust loadings may reach their maximums.

In addition to housing-level characteristics affecting lead levels and distributions in homes, several investigations of lead levels with relation to community characteristics were identified in this literature search. For example, Lanphear et al. (1998a) developed a model of community-level factors to examine whether community characteristics affected blood lead levels in 20,296 children tested in Monroe County, New York. Results of the analysis showed that the overwhelming majority of those with elevated blood lead levels lived in the city. For example, in the City of Rochester 37 percent of children tested had elevated blood lead levels, while only 4 percent of those living in areas around the city had elevated blood lead. Other community-level variables (some socioeconomic) that were associated in the model with increased risk of elevated blood lead levels in children included: lower housing value, older age of housing, higher population density, higher rates of poverty, lower percent of high school graduates, and lower rates of owner-occupied housing. The percent of housing built before 1950, which is a characteristic recommended by the CDC to identify at-risk communities, was also a significant risk factor for blood lead levels over 10 µg/dL. The authors concluded that community

characteristics can successfully be used to develop screening strategies for at-risk communities for lead hazards. Rabito et al. (2003) investigated the relationship between living in public housing developments and the risk of an elevated blood lead level among 7,121 high-risk children age 6 to 71 months in New Orleans. Public housing developments are specifically addressed under federal regulations to protect children from exposure to lead paint. Results of the study found elevated blood lead levels for 29 percent of children who were screened, but no differences between children residing in New Orleans housing developments and children in non-development housing. Margai and Henry (2003) utilized geostatistical methods to explore potential linkages between the prevalence of learning disabilities and pollution sources in an urban environment. Results of the analysis confirmed that areas of high risk for learning disabilities were strongly associated with historically significant sources of lead toxicity and air pollution facilities.

As lead is known to often be a particular risk for lower SES, inner-city children (e.g., due to older, dilapidated housing), Cory-Slechta et al. (2004) conducted a study on potential interactions between lead and another risk factor known to affect low SES women – stress. Results of this laboratory rat study, discussed previously in Section 3.1.3, showed that lead plus stress in pregnant females permanently elevated stress hormone levels in offspring, even when lead exposures were short-term. The authors suggest that such increases could suggest a potential new mechanism by which lead exposure could directly or indirectly enhance susceptibility to diseases and dysfunctions and induce cognitive deficits. Moreover, the authors note that the interactive effects of lead and stress, and particularly the potentiated effects of lead plus stress, raise questions about whether current risk assessment strategies sufficiently consider the true cumulative risk of inner-city lead exposures.

In addition to lead, other potentially neurotoxic substances such as mercury, arsenic, and arsenic derivatives (e.g., in chromium copper arsenate) may be found in residential environments.

Mercury. Mercury compounds (especially organic methylmercury, which elemental mercury is rapidly transformed to in the environment) are among the most potent developmental neurotoxicants. They can permanently damage the brain (e.g., causing mental retardation, cerebral palsy, and seizures), kidneys, and developing fetus at high levels of exposure (ATSDR, 1999b). Human exposures typically occur at low to moderate doses, however, and data on neurotoxic health effects at low doses are relatively limited (Davidson et al., 2004). An increasing body of evidence does suggests though that the developing brain is especially sensitive to methylmercury, with exposure levels that do not result in symptoms in pregnant experimental animals causing adverse effects to the offspring's development (Meyers and Davidson, 2000; NRC, 2000). Studies of human poisonings suggest this may also occur in humans (Meyers and Davidson, 2000; Mahaffey, 2000). In addition, consumer groups have recently raised questions about the potential link between mercury exposure (e.g., through the childhood vaccine preservative, thimerosal) and autism spectrum disorders as well as other adverse neurodevelopmental outcomes (Davidson et al., 2004). An independent review conducted by the National Academies of Science, National Research Council, concluded that, based largely on analysis of data from the three large epidemiological studies — the Seychelles, Faroe Islands, and New Zealand studies — low-level exposures to methylmercury *in utero* can have adverse effects on neurobehavioral development (NRC, 2000).

Although most researched exposures to date have focused on dietary sources (especially fish) as the most important pathways of methylmercury exposure (Mahaffey, 1999), recent studies show that mercury exposure may increasingly be an issue in domestic settings as well. In a review of the literature conducted by Counter and Buchanan (2004), additional potential sources of mercury identified included: elemental mercury vapor exposure through accidents (e.g., thermometer breakage), occupational and ritualistic use of elemental mercury (e.g., folk medicine practices, especially among inner-city immigrant populations); inorganic mercury exposure through the use of topical mercury-based skin creams and in infant teething powders; and metallic mercury in dental amalgams. Although no literature was found in the course of this review confirming residential exposures such as these, mercury is potentially present in the home in a wide variety of consumer products, such as control components in household appliances (e.g., gas ranges, grills, water heaters, furnaces, washing machines, gas dryers, older microwave ovens, portable phones), automobile components (e.g.., headlights, switches), old paint, cleaners (certain scouring powders, dish soaps, face soaps, etc.), computers (e.g., LCD computer screens, body of computer), electric equipment (e.g., switches, button cell batteries), lamps (e.g., fluorescent, High Intensity Discharge), personal care products (e.g., contact lens solution, eye and ear preparations, nasal sprays, etc.), and miscellaneous recreational products (e.g., lighted sneakers, toys, greeting cards, jewelry, cameras, etc.) (Draft Wisconsin Mercury Sourcebook, 2004; IMERC, 2004; Kuiken, 2002). Highlighting the potential issue of mercury in consumer products, several consumer groups and state governments recently called for a ban on all mercury-containing toys and novelties. This call for action was specifically prompted by news in June 2004 that Kellogg's company was putting a promotional toy containing mercury in several of its children's cereals (Frosted Flakes, Rice Krispies and Apple Jacks) in a battery to illuminate a Spiderman wrist gadget. Keebler, an affiliate, was offering a similar toy through a mail-in offer. Kellogg agreed to stop distributing the Spiderman toy nationwide and agreed not to use mercury in any future promotions (http://www.mercurypolicy.org/new/documents/KelloggSpiderManMercuryRelease071504nrdcmpp.pdf)

Arsenic and Chromium Copper Arsenate. Arsenic is a toxic element known to cause adverse health effects in humans, including nervous system, gastrointestinal, cardiovascular, and hematological effects, as well as skin and internal cancers in people exposed to levels greater than 300 ppb (ATSDR, 2000a). For most people, the major exposure to arsenic comes from food, although localized cases of chronic arsenic poisoning due to natural contamination of ground water and wells have also been documented (Ahmad et al., 2001; Calderon et al., 2004). In addition, other potential sources of arsenic may be present in residential settings. This may include exposure to inorganic arsenic compounds used in wood preservatives (i.e., chromated copper arsenate (CCA)), arsenic exposure due to proximity to industry/metals processing facilities, or proximity to areas where arsenic-based pesticides were used.

Although the potential magnitude of children's exposures to arsenic due to any of these residential sources is largely unknown, some researchers suggest that available information warrants concern. Belluck et al. (2003) conducted a critical review of available data on arsenic exposure, toxicology, natural and anthropogenic releases to soils, concentrations in background and contaminated soils, and regulatory toxicology. The authors found that arsenic releases to surface soils (via, e.g., air emissions, waste recycling, soil amendments, direct pesticide

application, and CCA-treated wood) often result in greatly elevated arsenic levels, sometimes one to two orders of magnitude greater than applicable numerical exposure standards. Furthermore, the authors note that although exceedances such as these at industrial or hazardous waste sites would result in regulatory actions, no similar actions are seen at residential and public spaces.

Estimated amounts of inorganic arsenic used in CCA-treated wood since 1975 total more than 300,000 metric tons, and most is estimated to still be in service (Bleiwas 2000, as cited in Belluck et al., 2003). Arsenic can be removed from the surface of CCA-treated wood by direct physical contact, although considerable uncertainty exists with respect to quantitative estimates of children's arsenic exposure from CCA-treated wood (Hemond and Solo-Gabriele, 2004). In addition, components of CCA may leach from the wood surface into the surrounding soil, thus elevating concentrations of arsenic, chromium, or copper in the vicinity of CCA-treated wood structures (Chirenje et al., 2003)

In 2003, EPA announced that although they were not able currently to make a finding of unreasonable risk to the public from CCA-treated products, limitations in residential uses of CCA would result in desirable reductions in arsenic exposure (http://www.epa.gov/pesticides/factsheets/chemicals/cca_transition.htm). In coordination, industry voluntarily agreed to move away from the use of pressure-treated wood that contains arsenic in new consumer products, and as of January 1, 2004, EPA does not allow CCA products to be used to treat wood intended for residential uses (including wood used in play-structures, decks, picnic tables, landscaping timbers, residential fencing, patios, gazebos and walkways/boardwalks). Wood treated prior to January 1, 2004, however, can still be used in residential settings. Additionally, structures containing CCA-treated wood that were already built prior to this action are not affected. Therefore, because CCA was widely used in the fabrication of outdoor decks and playground equipment prior to EPA's current restrictions, CCA treated wood may still be common in residential settings.

Several studies found in this literature search, including one review study, attempted to characterize potential releases from CCA-treated wood. In a review of data from the existing literature, Hemond and Solo-Gabriele (2004) estimated that arsenic doses in amounts of tens of micrograms per day may be incurred by children having realistic levels of exposure to CCA-treated decks and playground structures. Oral ingestion of arsenic dislodged from the wood by direct hand contact and then ingested via hand-to-mouth activity appeared to be the most important exposure pathway cited in the literature, followed by dermal absorption. Research indicated that ingestion of soil contaminated by arsenic leached from CCA-treated wood was a relatively minor pathway, except in cases where children exhibit pica (Hemond and Solo-Gabriele, 2004).

Stilwell et al. (2003) conducted a laboratory simulation study using a series of wipe samples to determine amounts and trends over time of dislodgeable arsenic (as well as copper and chromium) from CCA-treated wood surfaces. Over a 2-year period, the amount of dislodgeable arsenic had a high variability and did not follow a simple pattern – arsenic dislodged tended to decrease during the first year, but then increased somewhat during the second year. The authors hypothesize this increase was the result of surface rejuvenation effects caused by weathering and

surface erosion. The study also indicated that arsenic in CCA-treated wood may remain available for a number of years (Stilwell et al., 2003).

Regarding potential soil pathway exposures, Chirenje et al. (2003) studied copper, chromium, and arsenic distributions in soils adjacent to pressure-treated decks, fences, and utility poles ranging from about one year to twelve years in age in Florida. Analysis of lateral surface soil samples showed elevated concentrations of all three CCA components close to and under the structures (with the greatest impact within the first 0.3 m), with new structures exhibiting higher concentrations in surface soils than older structures. In some cases, arsenic soil clean-up action levels for the state were exceeded in areas directly surrounding structures. In relatively new structures, concentrations of arsenic, copper, and chromium quickly decreased as distance (e.g., at 1.5 meter) from the treated wood increased. Variations in soil concentrations were also apparent locally, depending on environmental factors such as soil type and weathering factors. For example, soils with low retention capacities (e.g., sandy soils with low organic matter) had lower arsenic levels in general due to increased susceptibility to leaching, and samples collected from underneath decks actually had higher arsenic concentrations than samples collected adjacent to the same decks, presumably due to lower rainfall (and thus leaching) underneath the deck. This study emphasizes the importance of considering local environmental factors, such as site characteristics and climate differences, in exposure studies.

In residential areas, CCA-treated wood has also been commonly used to construct raised garden beds. To investigate the potential for this use to serve as a pathway of exposure (including potential cases of food crop uptake) Rahman et al. (2004) conducted a controlled garden experiment. The study showed that although arsenic, copper, and chromium diffuse into soil from CCA-treated wood used to construct raised garden beds, and concentrations of arsenic in all crops (carrot, spinach, bush bean, buckwheat) grown in contaminated soils were higher than those from control soils, the concentrations of arsenics in the crops remained well below the recommended limit for arsenic in foods set by the United States Public Health Service (2.6 mg/kg fresh weight).

Beyond the intentional use of CCA-treated wood for residential structures, children may also come into contact with arsenic (and other metals) via landscaping mulch that contains recovered waste wood from construction and demolition debris. Townsend et al. (2003) performed leachability tests for chromium, copper, and arsenic on a variety of processed wood mixtures in Florida. Results of the tests showed that 18 of 22 samples collected from construction and demolition debris processing facilities leached arsenic at concentrations exceeding Florida's Groundwater Clean Up Target Level (50 µg/L). Furthermore, using a mass balance approach, the researchers estimated that mulch containing less than 0.1% CCA-treated wood would likely exceed Florida's residential clean soil guideline for arsenic (0.8 mg/kg).

In addition to arsenic exposure via CCA-treated wood, children may also potentially be exposed to arsenic from soils and dusts from nearby industrial and hazardous waste sites. Meyer et al. (1999) assessed the indoor exposures of children aged 5 to 14 years old living in an eastern German city with a long history of mining and smelting of nonferrous ores by measuring levels of lead, cadmium, and arsenic contamination in settled house dust. Results of the study indicated that a number of housing, neighborhood, and social factors were related to metal

loading rates in house dust and/or house dust loading rates. Of these, the area of residence was the most significant factor associated with arsenic levels in interior dust fall (this factor accounted for nearly half of the variances explained by the regression models). Loading rates were most elevated in the inner city areas, which are in closest proximity to the smelters and tailings piles.

Although EPA has cancelled all registered uses of inorganic arsenic for nonwood preservative purposes and in 1989 began to phase out household ant poisons containing sodium arsenate because of the danger of ingestion by small children, widespread past use in the U.S (particularly in orchards through the late 1940s) has left many current and former agricultural sites (some now converted to residential areas) with soil arsenic concentrations up to several thousand parts per million (Belluck et al., 2003). In addition, several (less toxic) organic arsenicals are still used today as herbicides primarily on cotton plants (99.5%), citrus, and sod (ATSDR, 2000a). Wolz et al. (2003) examined potential exposures for children living in an agricultural community in Washington with historic lead arsenate use from 1905 to 1947. Analysis of soil and house dust samples taken from 58 residences showed that homes near land that was used for apple or pear production between 1905 and 1947 had significantly higher soil arsenic than did the other homes, and 36 percent of these homes had soil or dust arsenic levels above the minimum risk level estimated by the Agency for Toxic Substances and Disease Registry. In addition to former orchards, farm fields, or other obvious agricultural areas, arsenic contamination due to past pesticide application may be present in current residential areas. For example, during the investigation of a Superfund site (former smelter) near Denver, Colorado, it was inadvertently discovered that a large area of residential Denver has soil arsenic levels in some areas exceeding a thousand parts per million due to the past use of an arsenical crabgrass killer and insecticide (PAX) in the 1950s and 1960s (Folkes et al., 2001). In the investigation, yard-by-yard soil sampling in residential areas around the smelter began in late 1993 to establish background arsenic levels, and within two years very high arsenic concentrations were found (e.g., a mean concentration of 141 ppm with several values greater than 1000 ppm). These levels often exceeded arsenic levels adjacent to the former smelter and Superfund site (e.g., 100 – 200 ppm), and were primarily in older neighborhoods that had well-established turf. The authors note that because PAX was widely distributed in the U.S., similar impacts may be observed in older neighborhoods in other cities where PAX was sold, depending on climate and soil conditions (e.g., the degree of leaching).

Pesticides. Pesticides are chemical agents used to control pests, and include insecticides (insects), herbicides (plants), fungicides (fungi), rodenticides (rodents), and acaricides (mites). Many common household products are also considered pesticides, such as kitchen disinfectants, products that kill mold and mildew, cockroach sprays and baits, rat poisons, and pet flea collars (Olkowski et al., 1991; EPA, 2002a). Some of the major classes of pesticides include organochlorines (e.g., aldrin, chlordane, pentachlorophenol), organophosphates (e.g., chlorpyrifos, diazinon, malathion), carbamates (e.g., carbaryl), synthetic pyrethroids (e.g., pyrmethrin), inorganic pesticides (e.g., boric acid), and others (e.g., botanical, microbial, and insect pheromones).

Use patterns for residential and agricultural insecticides have evolved over the last 50 years, during which time three major classes of compounds — the organochlorines, the

organophosphates, and the pyrethroids — have been used. Organochlorine pesticides, most notably DDT and chlordane, were widely used in the U.S. from the 1940s through 1970s. In 1972 use of DDT was phased out in the U.S. due to serious health and environmental concerns. DDT is still used in some countries for malaria vector control. Through the 1980s, chlordane was still approved for control of termites in homes and the pesticide was commonly applied underground around the foundations of homes.

With the banning of the organochlorines, the higher-cost organophosphate pesticides began to achieve widespread use for agricultural and residential pest control. While the organophosphates are less persistent in the environment, they are more acutely toxic to humans than organochlorines. During the latter half of the 1990s, it was estimated that 2 to 4 million pounds each of the organophosphate insecticides diazinon and chlorpyrifos (on the basis of active ingredients) were used annually by homeowners in the U.S. home and garden market (Aspelin and Grobe, 1999). Prior to their ban for home use, EPA estimated that approximately 75% of U.S. diazinon and 50% of U.S. chlorpyrifos was used for residential pest control (EPA, 2000a; EPA, 2001b). In June and November of 2000, EPA obtained agreements with manufacturers of diazinon and chlorpyrifos, respectively, to remove these chemicals from formulations used for indoor pest control (and diazinon from lawn and garden applications). These agreements were in response to developmental toxicity studies that found chlorpyrifos, and by implication, possibly the entire class of organophosphate pesticides, more toxic to infants, children, and pregnant or nursing women than was previously understood (Avakian, 2001). Several years prior to the total elimination of these products, EPA obtained agreements for the elimination of indoor-use foggers containing diazinon and chlorpyrifos after the identification of symptoms of acute pesticide poisoning in children when there was insufficient ventilation after application.

The ban on indoor products containing organophosphates led to the rapid introduction of pyrethroids for indoor pest control. The market is quite diverse with up to ten different pyrethroids being used in common products. These insecticides are widely viewed as "less toxic," although this assumption is based on the earliest pyrethroids that were botanicals derived from chrysanthemum flowers and had the advantage of low mammalian toxicity and very short environmental half-lives (Pesticide Profiles, 1997). However, formulations had poor shelf stability, especially when formulated as an aqueous spray. The search for more potent and longer-lived products led to the introduction of synthetic pyrethroids that were formulated to increase toxicity, increase resistance to degradation (either hydrolysis or enzymatic), decrease water solubility (Pesticide Profiles, 1997; Elliott, 1977; Itaya et al., 1977), and, by extension, enhance solubility in the human membranes, including those important to neurological function (Marei et al., 1982; Staatz et al., 1982).

Pesticide Use and Exposure. Roughly 90% of homes in the U.S. use chemicals to control pests (Landrigan et al., 1999). Approximately 2.2 billion pounds of pesticide active ingredients are used each year, or eight pounds for each man, woman and child in the U.S. (EPA, 1997; Natural Resources Defense Council, 1997). The EPA uses information from a variety of annual surveys to publish estimates on the production and use of pesticides in the United States. The most recently published report (EPA, 2002b) includes data on 1998-1999 market estimates. Table 3.2-2 presents the most common active ingredients in home and garden pesticides in 1999. The most recent restrictions on the use of certain pesticides, (e.g., chlorpyrifos) are not reflected

in the rankings of the most commonly used pesticides, but the inventory generally indicates that most pesticides are used in agriculture, with home and garden use accounting for less than ten percent of the total. The latest market estimate compilations from EPA are presented online, as available, at http://www.epa.gov/oppbead1/pestsales/.

Table 3.2-2. Most Commonly Used Pesticide Active Ingredients Home and Garden[1] Market, 1999 (Ranked by Range in Millions of Pounds of Active Ingredient)

1999 Rank	Active Ingredient	Type	Million pounds active ingredient	Chemical class
1	2,4-D	Herbicide	7 - 9	Chlorinated phenoxy compound
2	Glyphosate	Herbicide	5 - 8	Plant hormone-type
3	MCPP	Herbicide	3 - 5	Hormone-type phenoxy
4	Dicamba	Herbicide	3 - 5	Benzoic acid type
5	Diazinon	Insecticide	2 - 4	Organophosphate
6	Chlorpyrifos [2]	Insecticide	2 – 4	Organophosphate
7	Carbaryl	Insecticide	2 – 4	Carbamate
8	Benefin	Herbicide	1 – 3	Dinitrotoluidine
9	Malathion	Insecticide	1 – 3	Organophosphate
10	DCPA	Herbicide	1 – 3	Phthalate

Note: Includes applications to homes and gardens by professional applicators. Does not include moth controls: Paradiclorobenzene (30 - 35 million pounds per year) and naphthalene (2 - 4 million pounds per year). Also does not include insect repellent N,N-diethyl-meta-toluamide (5 - 7 millions pounds per year). Source: EPA proprietary data (EPA, 2002b).

[1] Garden herbicides would not be expected to have as much impact on home exposure as the insecticides used inside the house.

[2] Updated estimates, once available, will reflect the 2001 restrictions placed on chlorpyrifos use in residential settings.

Data also demonstrates that home and garden pesticide use has been increasing since 1995, reversing the trend of the last two decades. Herbicides used to kill lawn weeds are used more than other pesticides; six of the 10 most commonly used pesticides around the home are weed killers, and approximately 54 million pounds of herbicide active ingredient were used on lawns in 1999 (EPA, 2002b).

As part of the National Human Exposure Assessment Survey (NHEXAS), an evaluation of residential pesticide storage and use patterns was conducted in 308 Minnesota households with children aged 3-13. In-home interviews and inventories indicated that more than 850 unique products were currently being used. 97% of the homes had pesticides on the premises and 88% of households reported the use of pesticides, with no significant differences in residential storage and use patterns between households located in urban versus non-urban census tracts (Adgate et al., 2000). It has also been reported that in some urban areas, illegal street pesticides are also in use, including tres pasitos (a carbamate), tiza china, and methyl parathion (Landrigan et al., 1999).

Results of State and local waste pesticide collection and disposal programs (commonly known as Clean Sweep programs) also support the idea that there are large (but unquantified) amounts of pesticides, including many banned pesticides, that remain in storage in residential and agricultural settings and which could pose a serious environmental and human health threat if released (Fitz and Andreasen, 2002; EPA, 2002c). Based on data provided by the states, EPA estimates that Clean Sweep programs nationwide collected over 24.6 million pounds of

unwanted pesticides from 1980 through 2000 (Fitz and Andreasen, 2002). Pesticides turned in at Clean Sweep collection programs include canceled pesticides, such as DDT, which have not been sold in the U.S. for decades, as well as pesticides currently registered for use, such as 2,4-D. For example, from 1988 through 1998, Minnesota collected almost 95,000 pounds of several cancelled organophosphate pesticides (many associated with neurological effects), including aldrin, chlordane, DDT, dieldrin, mirex and toxaphene (EPA, 2002c). Forty-six states have conducted at least one Clean Sweep program, twenty-two states have conducted Clean Sweep programs for seven years or longer, and twelve states have ongoing programs (Fitz and Andreasen, 2002; EPA, 2002c). Since states with long-term, comprehensive Clean Sweep programs are still collecting pesticides, EPA believes that Clean Sweep programs will continue to be needed for the foreseeable future (EPA, 2002c).

Health Outcomes of Chronic and Acute Pesticide Exposure. The prevalence of pesticide use over the past several decades has raised significant concern over the health effects associated with both acute and chronic exposure to these compounds. In addition, studies conducted in the last 10 years have documented the presence of numerous different pesticides in indoor air, in carpet dust, and on settled dust of surfaces in homes (Rudel et al., 2003). These pesticides are present indoors at levels that are widely varying (Gordon et al., 1999; Nishioka et al., 1999; Roinestad et al., 1993; Simcox et al., 1995; Whitmore et al., 1994), and that on a compound by compound basis, often do not appear to constitute an immediate health risk. However, there are two major unknowns in the determination of potential health outcomes. First, the health impacts and outcomes from chronic pesticide exposures are unknown at this time (EPA, 2000b; Weiss, 2000). Second, there are generally multiple pesticides present in environmental media (e.g., dust, air) in and around the home. These include previously banned persistent organochlorine pesticides (e.g., chlordane, DDT), currently scrutinized organophosphate insecticides (e.g., chlorpyrifos) and newer, replacement pyrethroid insecticides. The cumulative effects of exposures to several compounds are not known. Given the toxicity of all insecticides toward some component of the nervous system (both central and peripheral nervous systems), it is believed that children are particularly at risk because complete development of the nervous system does not occur until late in childhood (Hall et al., 1997).

The most obvious adverse health outcome for children is poisoning from an accidental acute exposure to pesticides. In 2002, the American Association of Poison Control Centers documented 727,036 cases of nonpharmaceutical pediatric (<6 years of age) poisonings in the United States (Watson at al., 2003). Ninety-two percent of all of the exposures reported in 2002 occurred in the home. Of the total nonpharmaceutical pediatric poisoning cases, 7% (50,415) were attributable to pesticide exposures, although this may actually be an underestimate of the true number of cases each year due misdiagnosis – the symptoms between mild insecticide poisoning and the "flu" or other common ailments are often very similar. The symptoms of insecticide poisoning include headache, fatigue, dizziness, shortness of breath, and loss of appetite with nausea, vomiting, stomach cramps, and diarrhea (University of Nebraska Cooperative Extension, 1997). For very young children, the increased salivation, crankiness and loss of appetite due to mild pesticide poisoning may be often dismissed as "teething." Cases of acute pesticide poisoning are generally due to direct contact with a product via inadvertent ingestion, dermal contact, and/or inhalation. The majority of sub-acute poisoning cases (i.e., "mild poisoning" cases with flu-like symptoms) occur after indoor use of insecticides, such as in

homes or schools, and appear to be primarily due to either misapplication or a failure to fully ventilate the rooms after application. In studies examining such scenarios, levels of the insecticide chlorpyrifos were measured indoors on the day of application and the following day, and these data were combined with assumptions about exposure to estimate a dose for comparison with the NOEL (No Observable Effect Level; 30 µg/kg/day for chlorpyrifos) and the recently defined chronic exposure MRL (Minimum Risk Level; 1 µg/kg/d for chlorpyrifos) reported by the Agency for Toxic Substances and Disease Registry (ATSDR) (Fenske et al., 1990; Krieger et al., 2000; ATSDR, 2000b). Both studies found that the NOEL and chronic exposure MRL were in some instances exceeded in the short term.

Low-dose, chronic exposure may negatively impact the nervous system, though long-term effects are still not thoroughly understood. Animal data and in-vitro work suggest that chronic pesticide exposures might be tied to learning and behavioral problems, such as attention deficit hyperactivity disorder (ADHD) and other neuropsychological deficits (Chanda and Pope, 1996; Rice et al., 2000). In a review study conducted by Eskenazi et al. (1999), a significant body of animal research was found linking chronic low-level exposure to organophosphate chemicals with impaired neurodevelopment and growth in developing animals, affecting maze performance, balance, and locomotion in newborn and infant animals. Literature on health outcomes for farmers and farm workers routinely exposed to organophosphates was also identified, with symptoms such as headache, dizziness and sleepiness appearing to be associated with exposure, as well as some loss of peripheral nerve function (Eskenazi et al., 1999). Several major studies on health outcomes for very young children exposed to diazinon and chlorpyrifos were also funded by the National Institute of Environmental Health Sciences (NIEHS) and EPA prior to the phase out of these products (EPA, 2001a; EPA, 2000a; EPA, 2000c; Zartarian et al., 2000). Ruckart et al. (2004) examined children exposed to an agricultural organophosphate pesticide that was illegally used to control residential pests in Mississippi and Ohio. The authors found that some exposed children experienced difficulties with tasks involving attention and short-term memory, while parents of some exposed children reported behavioral and motor skill problems. However, these results were not consistent at both study sites, and exposed children performed just as well as unexposed children on tests of general intelligence, visual and motor skills, and multi-step cognitive processing. The authors could not conclusively attribute any neurobehavioral health effects to the pesticide studied (Ruckart et al., 2004). A review by Colosio et al. (2003) cautioned that despite the sheer volume of studies on chronic health outcomes associated with pesticide use, very few conclusions can be made. In most of the studies reviewed, no dose measurements were performed; some failed to even document the nature of the pesticide exposure on which the research was based.

*Pyrethroid Toxicity Studies***.** Even though research in the area of pyrethroid insecticides is only beginning, there is existing evidence on pyrethroid toxicity and the associated modes of action and metabolism that points toward the possibility of an association between pyrethroid compounds and adverse health outcomes. Evidence in support of this link follows.

There are two major classes of synthetic pyrethroids (Type I and Type II). Laboratory studies on the oral toxicities of Type I and II pyrethroids in rats, together with data on the toxicities of diazinon and chlorpyrifos, indicate that many pyrethroids approach the toxicities of the organophosphates (Kamrin, 1997; Miyamoto, 1976; Elliott, 1977; Worthing, 1983). The active

ingredient(s) of major insecticide products for in-home use may be either Type I or Type II pyrethroids, and many high volume products (e.g., Raid with 23% of the market share, Hot Shot with 16% of the market share) contain Type II pyrethroids (Market Share Reporter, 2001). Many current products for outdoor use are convenient-to-use aerosols and sprays that can easily be used indoors (against label directions), and these products contain both organophosphates and pyrethroids.

Extensive mammalian studies of organophosphate toxicity, in general, and chlorpyrifos toxicity, in particular, have suggested that neurotoxic effects can be expected from low dose/chronic exposures. In addition to inhibiting nerve transmission, organophosphates also interfere in the acquisition and development of new brain cells and inhibit DNA synthesis (Whitney et al., 1995; Dam et al., 1998; Li and Casida, 1998). These functions are critical to proper neurological development, especially in the cognitive realm (Rice and Barone, 2000; Weiss, 2000).

Research has indicated that the primary site of action for these insecticides is the central nervous system, rather than peripheral (Staatz et al., 1982). In a study of a high level exposure to permethrin, certain groups of rats showed significantly lower retention capacity, decreases in coordination and balance, and higher incidence of conflict behavior (Sherman, 1979). Finally, important studies have also demonstrated critical issues for neonatal exposures to pyrethroids. Cantalamessa (1993) found two pyrethroids, permethrin and cypermethrin, to be more toxic to the neonate compared with the adult rat. Sheets (2000) identified no difference between neonate and adult susceptibility for exposure to Type I pyrethroids but a three-fold difference for exposures to Type II pyrethroids. Sheets attributes this increased susceptibility in neonates to a limited detoxification capacity for Type II compounds, as well possibly the ability of Type II compounds to accumulate in biological tissues. Since initial pyrethroid exposures may occur early in life, when metabolic systems have limited capacity and exposures may have life-long implications, it is important to understand the frequency and magnitude of early childhood exposures, the routes by which these exposures occur, and the outcomes of such exposures.

Factors Affecting Pesticide Exposures in Residential Settings. Numerous housing factors and behavior patterns may affect the degree to which residents will be exposed to pesticides used in and around the home. Even with full implementation of pesticide use precautions, residues can remain in a home for years after use, and chronic exposures may occur (Whitmore et al., 1994). Factors promoting environmental degradation and dispersion (e.g., sunlight, wind, rain and microbes) are not readily available for completely dissipating indoor pesticide levels. This persistence in the indoor environment is further exacerbated by the presence of household materials such as carpets, upholstered furniture, and draperies. These act as sorbents or reservoirs resulting in subsequent slow release of the pesticides over time (Cohen Hubal et al., 2000; Pang et al., 2002). These chemical residues, if persistent, will continually cycle through the indoor reservoirs either by virtue of volatilization and reabsorption, or as a result of reservoirs being disturbed by activities such as cleaning or active play.

For example, prior to their cancellation, organochlorine termiticides (particularly chlordane) were used to treat many homes, soils, and building structures. Particularly during demolition or other disturbances, these reservoirs have the potential to be significant sources. Research shows that indoor air and house dust in structures previously treated with these persistent

organochlorines can have residual pesticide levels as much as 10-100 times higher than in outdoor air and surface soil (Lewis et al., 1988; Whitmore et al., 1994; EPA, 2000c; Wilson et al., 2003). Fortune et al. (2000) investigated the bioavailability of pesticide residues in aged carpets. The authors reported that carpet fibers and binder were the predominant reservoirs for pesticide residue, with carpet padding also retaining a small amount of residue. Very little residue was found on the carpet surface, suggesting that pesticide residues in carpet would not be easily dislodged (Fortune et al., 2000). Of greater impact to children may be reservoirs such as toys and pillows. Gurunathan et al. (1998) studied the accumulation of pesticide residue on children's toys and other surfaces following application of (now banned) chlorpyrifos. Results indicated that chlorpyrifos residue continued to accumulate on and in toys and other sorbent surfaces for two weeks following application, far exceeding the post-application reentry times suggested by manufacturer labels (1-3 hours). This resulted in an estimated nondietary dose of 208 µg/kg/day over the two week period for a 3 to 6-year-old child; children with a high frequency of mouthing behavior could be exposed to as much as 356 µg/kg/day (Gurunathan et al., 1998). A study by Lewis et al. (2001) found that pesticide residues were easily redistributed from application areas to surfaces accessible to humans and pets, with pesticide residues measured on children's toys and other indoor surfaces following outdoor diazinon and indoor chlorpyrifos application. Although residues on toys were much lower than in the Gurunathan study, residues found on children's hands indicated that frequent mouthing behavior could contribute as much as 1-1.5 µg/kg/day, which exceeds the EPA's reference dose for diazinon but not for chlorpyrifos (Lewis et al., 2001). Pang et al. (2002) investigated children's aggregate exposures to chlorpyrifos as part of the National Human Exposure Assessment Survey (NHEXAS) in Maryland. Indoor air, carpet dust, exterior soil, and duplicate diet samples from 80 individuals at various times over a year indicated that exposure from inhalation of indoor air accounted for 84.7% of aggregate daily exposure to chlorpyrifos on average, although short-term measurements of chlorpyrifos in air were highly variable over time. Chlorpyrifos concentrations in indoor air and carpet dust were significantly correlated, with carpet levels showing less variability over time.

Residential exposure to pesticides may occur even in areas of the home where pesticides were not used. For example, outdoor pesticides can be tracked indoors or penetrate the indoor environment through spray drift (Lewis et al., 2001). A pilot study by Nishioka et al. (1999) indicated that tracking may be a more important factor than spray drift in the distribution of lawn pesticides indoors. Median levels of the pesticides in indoor dust, measured at 0.5 $\mu g/m^2$ prior to application, remained between 0.5 and 2.0 $\mu g/m^2$ in unoccupied homes but ranged from 1.0 to 228 $\mu g/m^2$ in occupied homes following outdoor application. The authors suggested that tracking could be significantly reduced if residents removed their shoes at the door (Nishioka et al., 1999).

Neighborhood factors (e.g., rural/urban location) can also influence pesticide exposure risk. In a study that analyzed both dust samples and metabolite concentrations in urine, median house dust and metabolite concentrations of organophosphate pesticides were significantly higher among children who lived in an agricultural community than those who lived in a non-agricultural neighborhood. Furthermore, exposure levels of children whose parents use agricultural chemicals or who live near farmland treated with pesticides were found to be significantly higher than those of other children living in the same community (Lu et al., 2000). Other research has

indicated that pesticides are of particular concern in low-income, inner-city areas, where conditions favor pest infestation and, consequently, pesticide usage. Using both questionnaire and laboratory data, Berkowitz et al. (2003) found considerable exposure to indoor pesticides within a cohort of multi-ethnic, urban women. In an ongoing study conducted by Columbia University on the effects of indoor air pollutants on pregnant women and their newborns in minority communities within the New York City area, strong associations were observed between dilapidated housing and pesticide exposures. Results suggested widespread use of pesticides in these areas, with 85% of the women reporting the use of pest control techniques during pregnancy and 35% reporting that exterminators had treated their homes, nearly half of which were treated more than once per month. At least four pesticides were detected in the personal air samples of all women who consented to monitoring during their third trimester. In the case of diazinon, the exposure for some women may have exceeded health-based levels (Whyatt et al., 2002). The project also reported a high degree of correlation between maternal pesticide levels and levels found in cord blood samples, indicating that exposures are easily transferred between mother and fetus (Whyatt et al., 2003).

As can be seen, dermal, inhalation, and non-dietary ingestion exposures to organochlorine and organophosphate insecticides can continue to occur on a chronic basis. However, except in cases of gross misapplications, these chronic exposure levels will be overshadowed by the dietary ingestion of residue levels in foods. For the organochlorines, the dietary ingestion levels are driven by bioaccumulation in meat, fish, milk, and other high fat foods. For the organophosphates, the dietary ingestion levels are driven by those fruit, vegetable and grain products where agricultural uses are still permissible (EPA, 2003). In contrast to the phased-out organochlorines and organophosphates, currently used pyrethroids will dominate indoor residential pesticide exposures in the future. Pyrethroid pesticides are also being used to a greater extent in the agricultural arena, so that dietary exposures to these pesticides are expected to increase as well. In addition to the pesticidal active ingredient, adjuvants such as piperonyl butoxide, which is used to enhance the "knock-down" effect of pyrethroids, and inert ingredients such as solvents may cause health problems for sensitive individuals such as children, older adults, and people with chronic illnesses (Watson et al., 2003).

Other Organic Chemicals. Numerous other organic chemicals have been cited in the literature as having potential neurodevelopmental effects. The most frequently researched chemicals are polychlorinated biphenyls (PCBs), dioxins, and polybrominated diphenyl ethers (PBDEs), but numerous additional chemicals that are also suspected of having endocrine system effects are cited as having other developmental effects as well (see discussion Section 3.5.3 of this report). For the majority of industrial chemicals in use today, however, data on neurotoxicity is not available (Schettler, 2001). For example, there are currently over 80,000 chemicals registered for use in the U.S., and nearly 3,000 of those are High Production Volume (HPV) chemicals being produced in quantities greater than one million pounds per year. In response to several independent studies that found that very little basic toxicity data were publicly available on most of the HPV chemicals, EPA conducted a review and found that, of the approximately 3,000 non-polymeric, organic substances manufactured or imported in amounts equal to or greater than 1 million pounds per year based on 1990 reporting, only 7% had a full set of publicly available, internationally recognized, basic health (including neurotoxic effects) and environmental fate/effects screening test data, and 43% had no such information publicly

available (EPA, 1998; Goldman and Koduru, 2000). In addition, there was no screening level developmental toxicity information available for about 78% of all HPVs, or over 45% of HPV chemicals commonly found in consumer products (Goldman and Koduru, 2000).

Polychlorinated Biphenyls (PCBs). *In utero* and early life exposures to PCBs have been one of the most extensively investigated neurotoxic exposures in the literature. PCBs are a group of synthetic organic chemicals which were manufactured in large quantities in the United States from 1929 through 1979, and commonly used as coolants and lubricants in transformers, capacitors, and other electrical equipment, as heat-resistant hydraulic fluids, and as heat-conducting fluids in heat exchangers, as well as a variety of consumer products, ranging from fluorescent lighting fixtures and small capacitors in appliances (e.g., microwaves), to microscope oil, ink, caulking compounds, carbonless copy paper, plastics and plasticizers, paints, adhesives, flame retardants, and pesticide carriers. Due to their persistence, PCBs are distributed widely in the environment from past uses, including at high concentrations in some localized areas due to industrial contamination (e.g., Anniston Alabama). In addition, although PCBs can no longer be manufactured, many older transformers and capacitors may still contain PCBs, and this equipment can be used for 30 years or more. PCBs may also be present in old consumer products still in use, such as old fluorescent lighting fixtures, and old electrical devices and appliances such as television sets and refrigerators (ATSDR, 2000c). Indoor air concentrations of PCBs may be elevated when these electric devices get hot during operation and volatilize PCBs; the devices may also leak as they get older and serve as a source of dermal PCB exposure (ATSDR, 2000c). The main pathway of PCB exposure for the general population, however, is via the consumption of contaminated food, primarily fish.

Laboratory studies have established that PCBs are neurotoxins in animals exposed pre- and post-natally, even at low doses (ATSDR, 2000c; Longnecker et al., 2003). Human data regarding PCB exposures early in life and neurotoxic effects is more limited, and difficult to interpret due to differences in quantification across studies (Longnecker et al., 2003). Information on potential human health effects includes several studies of women accidentally exposed to higher levels of PCBs, as well as investigations of neurological effects in children exposed to background levels of PCB exposure (i.e., levels of exposure experienced by the general population).

For example, longitudinal studies have been conducted on children of about 2,000 Taiwanese people accidentally exposed to PCB-contaminated cooking oil in 1979 (i.e., the Yu-cheng cohort). Observed health effects of high-level prenatal PCB exposure in this population include reduced intelligence/delayed development, retarded growth, physical abnormalities, and sperm abnormalities in young boys and men after puberty (also see discussion in Section 3.5.3 of this paper on endocrine disruption) (Guo et al. 2004).

A series of studies have been conducted on a cohort of women who consumed high amounts of Lake Michigan fish contaminated with PCBs. In initial investigations, children whose mothers had eaten PCB-contaminated fish demonstrated abnormal responses to tests of infant behavior (e.g., hypoactive reflexes, motor immaturity, and a greater amount of startle) (Jacobson et al. 1984), poorer performance on both the Verbal and the Memory scales of the McCarthy Scales of Children's Abilities at age 4 (Jacobson et al., 1990), and lower IQ and reading comprehension scores at age 11 years (Jacobsen and Jacobson, 1996; Jacobson and Jacobson, 2004). Jacobson

and Jacobson (2004) investigated which specific elements of cognitive function were primarily affected in the Lake Michigan cohort and observed that although deficits in digit cancellation, memory, lack of impulsivity control, and reaction time tests, other measures of cognitive function (e.g., visual-spatial rotation efficiency) were not affected at age 11 years. Also of note in the study, adverse cognitive effects were much more frequent and also more marked in children who were not breast fed, even though breast milk contamination with PCBs would be expected to increase postnatal PCB exposures. The authors note that it is unclear whether the apparent protective effect of breast feeding is related to nutrients in breast milk or to a higher quality of intellectual stimulation that often is provided by mothers who breast feed their infants (Jacobson and Jacobson, 2004). Some, however, have noted that the reliability of the Michigan cohort studies may be limited but the fact that the women may have been exposed to other chemicals (ATSDR, 2000c).

Patandin et al. (1999) studied possible adverse cognitive effects in 395 young Dutch children exposed *in utero* and via breast milk to environmental "background" levels exposures to PCBs and dioxins. Cognitive abilities were assessed with the Kaufman Assessment Battery for Children in 42-month-old children and verbal comprehension was assessed with the Reynell Language Developmental Scales. Results suggested that maternal exposure to background levels of PCBs was associated with lower scores on the cognitive test. Current and breast milk exposures to PCBs and dioxins were not related to 42-month cognitive performance.

Regarding other potential sources of PCB exposure for children, several recent studies have also investigated PCBs in building materials such as plaster and caulk. Although these uses have been discontinued for many years, it is believed that, similar to lead paint, these materials may still be present in some older structures. Herrick et al. (2004) investigated 24 buildings (including schools and other public buildings) in the Greater Boston Area and found that one-third contained caulking materials with PCB content exceeding 50 ppm by weight, which is the USEPA limit for a material to be considered a PCB bulk product waste. In one building indoor air levels of PCB were elevated to levels that triggered EPA to mandate removal and clean-up measures. Several European studies have also had similar findings regarding PCBs in building materials in Norway and Demark (where PCBs have also been banned for years). Andersson et al. (2004) investigated the extent and distribution PCB in plaster on building facades of homes and public buildings in Norway by sampling surface soil, plaster, and paint from structures built between 1952 and 1979. Results showed that adjacent to buildings with PCB-containing plaster, 30 percent of the soil samples had a PCB concentration that exceeded the Norwegian action level. PCB concentrations were higher in both soil and plaster of residential buildings and schools than buildings designated for office use, storage, or for industrial purposes. Higher PCB concentrations were also observed in buildings built in the 1950s and 1960s in comparison to newer (1970s) buildings when the usage of PCBs for these purposes decreased. Soil samples tended to have higher PCB concentrations than the corresponding plaster from adjacent walls, which the authors suggested is likely due to the higher organic matter content of soils (and thus ability to retain PCBs). In a study of PCBs in caulk in Denmark, Wilkins et al. (2002) found PCBs in dust from buildings with PCB-containing caulk to be 10-20 times the amounts found in samples from other buildings

Brominated Flame Retardants (BFRs). In recent years, findings that BFRs such as polybrominated diphenyl ethers (PBDEs) and polybrominated biphenyl (PBB) are ubiquitous in

environmental media, wildlife, and in humans (ATSDR, 2002) have led to increasing concerns about their potential health effects (Birnbaum and Staskal, 2004). BFRs are manufactured chemicals that have been used for decade in plastics and a variety of consumer products (e.g., computer monitors, televisions, textiles, plastic foams, etc.) to inhibit burning. The use of PBBs has been discontinued since the 1970s. Although animal studies indicate that BFRs can cause disruption or the nervous system (as well as the immune systems, liver, kidneys, and thyroid gland), the data on human exposures and health effects is very limited (ATSDR, 2002). Nervous system disruptions observed in animal studies include behavioral alterations, deficits in learning and memory, and pronounced hyperactivity into adulthood (Branchi et al., 2003).

Pentachlorophenol/Dioxins. Dioxins (polychlorinated dibenzo-para-dioxins, or PCDDs) and furans (polychlorinated dibenzofurans, or PCDFs) are a group of toxic chemical compounds which are generated and released into the environment as by-products of various combustion and chemical processes. Due to their toxicity, tendency to bioaccumulate, and persistence in the environment, dioxins have been the subject of ongoing public health and environmental concern. Despite existing controls, they are distributed widely at low levels in the environment, sometimes at levels which may pose risk. For example, dioxins have been the cause of numerous fish consumption advisories in the U.S. Great Lakes region and Ontario, and the EPA has recently estimated that the risks for the general population based on dioxin exposure could be as high as the range of a 1 in 100 to 1 in 1,000 increased chance of experiencing cancer related to dioxin exposure (EPA, 2000d). In addition to cancer effects, dioxin has been reported to result in neurological symptoms (e.g., peripheral neuropathy) in accidental human exposures (e.g., industrial explosion in Seveso, Italy and spraying of waste oil contaminated with dioxins on roads in Missouri), as well as a plethora of other health symptoms in animal studies (ATSDR, 1998). The majority of dioxin exposure typically occurs through the food chain, primarily animal fats (meat and dairy) (EPA, 2000d). However, evidence also suggests that significant amounts of dioxin compounds are produced annually as a contaminant of pentachlorophenol (PCP), a wood preservative, and are tied up in PCP-treated products (EPA, 2000d). In addition to dioxin-like health effects due to dioxin contaminants, acute exposure to relatively high levels of PCP have been reported in human cases and animal studies to cause harmful effects on the liver, kidneys, blood, lungs, nervous system, immune system, and gastrointestinal tract (e.g., in accidental poisonings of sawmill workers). Long-term exposure to low levels of PCP (e.g., chronic occupational exposures, people living in log homes treated with PCP-containing wood) have been reported to cause damage to the liver, kidneys, blood, and nervous system (ATSDR, 2001).

The only currently permitted use of PCP in the U.S. is as a wood preservative in utility poles and crossarms, but the EPA's current assessment of PCP indicates that the most significant mass of PCP is present in utility poles. It is estimated that there are in excess of 120 million treated-wood utility poles in place in the United States, and since PCP has been the dominant preservative used for the treatment of utility poles in the last 25 years, many of these poles are treated with PCP. A treated utility pole can be expected to last for approximately 30 years (AWPI, Penta Council). In addition to exposures to PCP/dioxins from in-use utility poles, there is also concern regarding the secondary use market – poles that are no longer acceptable for carrying power lines are often sold to consumers for use e.g., as fence posts, landscape materials, or supports for vehicle shelters.

Lorber et al. (2002) conducted a study to estimate the rate of environmental release of dioxins from in use PCP-treated utility poles via leaching and volatilization. By comparing the dioxin congener distributions in cross sections of poles of varying ages, it was found that dioxin concentrations were consistently higher in the outer portions of the poles than the center, particularly in older poles. The authors suggested that this trend for dioxins to concentrate in the outer portions of the pole over time may result in environmental release of dioxins from PCP-treated poles over time.

In a series of studies, Dahlgren et al. (2003a and 2003b) investigated the health effects and potential dioxin exposure of residents of a nearby wood treatment plant that had used creosote and PCP to treat wood for over 70 years. Results of environmental sampling of soil and sediment samples from drainage ditches, attic/dust samples and kitchen wipes from nearby residents' homes (n= 10) suggested a significant contamination of the neighborhood by wood processing waste chemicals (Dahlgren et al., 2003a). Blood was also sampled from ten residents and test results showed elevated values for several dioxin congeners, compatible with PCP as the source (Dahlgren et al., 2003a). Based on questionnaires and physician histories, adverse health effects also appeared to be more prevalent in long-term residents near the wood treatment plant, with residents reporting significantly more cancer, respiratory, skin, and neurological health problems than the controls (Dahlgren et al., 2003b). Physician administered neurological testing also suggested significantly more neurophysiologic abnormalities in adults of reaction time, trails A and B, and visual field defects (Dahlgren et al., 2003b).

Carbon Monoxide. Carbon monoxide (CO) is a poisonous gas produced as a by-product of incomplete combustion of carbon-based fuels such as natural or liquefied propane (LP) gas, kerosene, oil, wood, or coal. CO is poisonous primarily because it interferes with oxygen transport to the tissues and organs of the body and leads to adverse health effects, particularly in sensitive organs such as the brain. Initial symptoms of acute exposure to higher levels of CO can begin with central nervous system (CNS) effects such as a headache, dizziness, weakness, nausea, vomiting, disorientation, and confusion, as well as other symptoms such as shortness of breath (Raub and Benignus, 2002). If exposures continue, symptoms become more intense, progressing to collapse, a loss of consciousness, or even death. At lower CO concentrations, CNS effects can include subtle sensory-motor deficits such as reduction in visual perception, manual dexterity, learning, driving performance, and attention level (Raub and Benignus, 2002). Survivors of CO poisoning may also have long-term neurological effects such as personality changes, memory deficits, impaired judgment, poor concentration, and other intellectual impairments (Varon and Marik, 1997; Raub et al., 2000; EPA, 2000). In addition, symptoms may not appear until days after exposure. These delayed symptoms, which can appear up to 40 days after exposure, are referred to as delayed neurological sequelae of CO poisoning (Townsend and Maynard, 2002). Some researchers suggest that prolonged exposure to CO, even at levels previously believed to be low, is capable of producing numerous, and persistent, adverse physical, cognitive, and emotional health effects in humans (Penney, 2000; Devine et al., 2002; Liu et al., 2003).

In addition, research indicates that CO may have adverse health effects beyond those related to oxygen depletions, such as interference with biological pathways in cells (Devine et al., 2002;

Townsend and Maynard, 2002). Although controversy exists over the role other processes may play in either acute or chronic CO poisoning, phenomena such as delayed neurological sequelae cannot be explained by hypoxia alone (i.e., after blood oxygen levels have returned to normal, symptoms would be expected to improve) (Townsend and Maynard, 2002). While the role of other processes or the effects of CO on cellular function are not well understood, evidence suggests that hypoxia, per se, might not be the only process involved in CO pathology (Townsend and Maynard, 2002).

As much of the concern with CO health effects are regarding acute poisonings, major potential CO sources in residential situations and conditions that can lead to elevated CO concentrations in homes are discussed in Section 3.3.4 on injury. Common sources of elevated CO levels in homes include malfunctioning or improperly vented gas heating systems or other combustion appliances, and cars that are left running in attached garages.

3.2.5 Biological Attributes of Housing/Neighborhoods Associated with Neurobehavioral Development, Developmental Disabilities and Psychiatric Outcomes

Mold. Although the focus of the literature on residential mold exposures is primarily regarding inhalation exposures and potential asthma exacerbation and other adverse respiratory health effects, molds have also been reported to act as neurotoxins in certain exposure scenarios (Kelman et al., 2004; Bennett and Klich, 2003). Under the appropriate environmental and competitive conditions (e.g., in the presence of water-soaked cellulosic materials) molds can produce mycotoxins (Burge and Amman, 1999), many of which have been associated with adverse neurologic effects, as well as numerous other adverse responses (e.g., immunotoxic and dermal responses, cancer, etc.) (Bennett and Klich, 2003). The majority of the data regarding neurological effects, however, is from animal studies or human poisoning cases due to the ingestion of mycotoxin-contaminated food (e.g., peanuts and grains in third world countries with humid climates) (Bennett and Klich, 2003).

In a review of the literature through 2003 on molds and health effects conducted by the National Academies of Sciences IOM, findings indicated that although there is sufficient data from animal models and human epidemiological data to conclude that mycotoxins pose an important danger to human health, there is inadequate or insufficient information to determine whether molds or the specific chemical agents associated with them (e.g., mycotoxins) are related to neuropsychiatric health outcomes in residential exposure scenarios (NAS, 2004).

In other literature reviews conducted recently, reviewers have also reached similar conclusions. Hardin et al. (2003) reviewed recent literature and concluded that current scientific evidence does not support the proposition that human health has been adversely affected by inhaled mycotoxins in the home, school, or office environment, despite the fact that adverse effects of molds and mycotoxin exposure from ingestion of contaminated foods are widely recognized (Hardin et al., 2003). Fung and Hughson (2003) also examined the current data on indoor mold exposure (visible survey or objective sampling) and human health effects published from 1966 to November 2002. Although they found that current evidence does support the relationships between excessive moisture, mold growth, and increased prevalence of symptoms due to irritation, allergy, and infection, specific human toxicities due to inhaled fungal toxins were not scientifically established. In another investigation of the likelihood of adverse (non-allergic)

health effects due to mycotoxin exposure, Kelman et al. (2004) developed a model of the maximum possible dose of mycotoxins that could be inhaled in 24 hours of continuous exposure to a high concentration of mold spores containing the maximum reported concentrations of several known toxic mycotoxins (e.g., aflatoxins B1 and B2, satratoxins G and H, fumitremorgens B and C, verruculogen, and trichoverrols A and B). The modeled doses indicated that none of the maximum doses were sufficiently high to cause any adverse effects, which the authors suggest is further evidence that toxic human health effects following inhalation exposure to mycotoxins in mold-contaminated home, school, or office environments is implausible.

In contrast, in an evaluation of mold-exposed individuals, Kilburn (2003) found preliminary evidence to suggest that indoor mold exposures were associated with neurobehavioral and pulmonary impairments that likely resulted from the presence of mycotoxins, such as trichothecenes. In the study, the author conducted neurological evaluations of 65 individuals (40 families) from Arizona, California, and Texas exposed to mold in their homes (as established by visible mold growth on walls, cultured indoor air samples, and presence of mold or mycotoxin antibodies in blood serum samples). In comparison to a non-exposed reference group (n=202), the mold-exposed group exhibited decreased function for balance, reaction time, blink-reflex latency, color discrimination, visual fields, and grip, and reduced scores on digit-symbol substitution, peg placement, trail making, verbal recall, and picture completion tests. Many of the subjects also exhibited pulmonary impairments. Another small study conducted by Anyanwu et al. (2003) assessed possible neurophysiological effects in ten children who attended a health center because of chronic indoor toxic mold exposure. Results of clinical neurological and neurobehavioral questionnaires administered to the children's parents and a series of objective neurophysiological tests, including electroencephalogram (EEG), brainstem evoked potential (BAEP), visual evoked potential (VEP), and somatosensory evoked potential (SSEP), suggested significant neurological deficits in all the patients compared to controls.

The primary housing factors affecting fungal growth in homes are discussed later in Section 3.4 on asthma and other adverse respiratory effects.

Infection. Very limited literature regarding possible associations between infection and neurodevelopmental or neurobehavioral outcomes was identified in this search. One study, Brown et al. (2004) investigated whether serologically documented prenatal exposure to influenza increases the risk of developing schizophrenia later in life. It did not, however, relate this exposure to housing or neighborhood characteristics. According to the authors, previous studies investigating this issue had relied on maternal recall only. In a large birth cohort born from 1959 through 1966 (in which 64 members were diagnosed as having schizophrenia spectrum disorders and 125 were not), archived maternal serum was analyzed for influenza antibody. Results of the analysis indicated that the risk of schizophrenia was increased 7-fold for influenza exposure during the first trimester, but no increased risk during the second or third trimesters.

3.2.6 Neighborhood Attributes and Other External Factors Associated with Neurobehavioral Development, Developmental Disabilities and Psychiatric Outcomes

General Community Health. A significant amount of literature examining the role of community level factors, independent of individual characteristics, on neurobehavioral, neurodevelopmental, and psychiatric outcomes was identified in the literature search. In addition to overall community characteristics, community level factors addressed in the literature included location, noise, and neighborhood safety.

Cognitive Outcomes. Neighborhood characteristics were examined in relation to cognitive outcomes and academic achievement in several studies identified in this literature search. The potential influence of selected collective neighborhood characteristics on rates of childhood learning disabilities (LD) were investigated by Margai and Henry (2003) in a study that used geo-statistical methods. Primary data on childhood learning disabilities for 1997 were analyzed to identify spatial clusters within the community. Results indicated that areas of high risk for LD were strongly associated with historically significant sources of lead toxicity and air pollution facilities, the presence of multiple/subdivided housing units, poverty, higher percentage of residents on public assistance and lower adult educational attainment. Baker and Davis (2001) attempted to use indicators of community health to investigate adolescent academic achievement. Using modeling techniques, school district community contextual variables (including community education level, percentage of children in poverty, teenage pregnancy rate, percentage of single-headed households, and rate of low birth weights) were compared to standardized test results for 8th grade students. The community models accounted for up to 63% of the variance in adolescent academic achievement. Leventhal and Brooks-Gunn (2004) studied neighborhood effects on educational outcomes in 588 low-income children in New York City who were moved from high- to low-poverty neighborhoods as part of the Moving to Opportunity for Fair Housing Demonstration program. Analysis of data on the children' academic achievement, grade retention, and suspensions/expulsions after 3 years indicated that moving to low-poverty neighborhoods had positive effects on 11-18-year-old boys' achievement scores compared with those of their peers in high-poverty neighborhoods. The scores of male adolescents in low-poverty neighborhoods were comparable to females' scores, whereas male adolescents' scores in high-poverty neighborhoods were 10 points lower than female peers.

Mental Health Outcomes. Several studies identified in this literature search also examined neighborhood characteristics in relation to mental health outcomes. In another New York City study as part of the Moving to Opportunity for Fair Housing Demonstration, Leventhal and Brooks-Gunn (2003) examined the effects of neighborhood on mental health. Measures of mental health were assessed in 550 families who moved from public housing in high-poverty neighborhoods into private housing in near-poor or non-poor neighborhoods (with a subset remaining in public housing). At the end of 3 years, parents who moved to lower poverty neighborhoods reported significantly less distress than parents who remained in higher poverty neighborhoods, and boys who moved to less poor neighborhoods reported significantly fewer anxious/depressive and dependency problems than did boys who stayed in public housing. Using data from the National Institute of Mental Health's Epidemiological Catchment (ECA) surveys of 11,686 individuals in New Haven, CT, Baltimore, MD, St. Louis, MO, Durham, NC, and Los Angeles, CA, Silver et al. (2002) examined the relationship between neighborhood

structural characteristics (including socioeconomic disadvantage, racial/ ethnic heterogeneity, and residential mobility) and mental disorder. Results of the analysis showed higher rates of major depression and substance abuse in individuals from disadvantaged neighborhoods, after controlling for individual-level characteristics. In addition, higher rates of schizophrenia, major depression, and substance abuse were associated with neighborhood residential mobility. In an ecological study of 107 U.S. cities, Cohen et al. (2003a) found that neighborhood physical conditions (as indicated by boarded-up housing) may be related to premature mortality (from a number of causes, but including suicide and homicide) because of their potential adverse influence on social relationships and opportunities for healthful behaviors. Yang (2000) also examined mental health in relation to neighborhood experience and community characteristics in a study of 416 subjects from five urban, suburban, and rural communities in southern Taiwan. Measurements of mental health and perceptions of neighborhood were collected via questionnaire, and other community characteristics (including population density, community socioeconomic condition, and community stability) from government archived data. Analysis of the data showed that personal income, community socioeconomic condition, and perceived social support from the neighborhood were statistically significant when associated with a person's mental health status. Although several of these studies focused on adults, they still provide evidence that the structural characteristics of neighborhoods affect the prevalence of mental disorders.

Disadvantaged Neighborhoods, SES, and Stress. Possible mechanisms for general health effects in socioeconomically disadvantaged neighborhoods, including cumulative stress, were also examined in several studies. Ellen et al. (2001) conducted a review of research on the topic and found that it is difficult to differentiate whether the poorer health observed in disadvantaged neighborhoods is primarily a function of lower socioeconomic status (SES), or whether there are additional factors in disadvantaged neighborhoods that contribute to the effect. Although they note that methodological issues make the literature inconclusive, they authors hypothesize that neighborhoods may primarily adversely affect human health in two ways: 1) through short-term influences on behaviors, attitudes, and health care utilization, and 2) through long-term accumulated stress, lower environmental quality, and limited resources of poorer communities. The authors suggest that through the second mechanism, the health of residents is eroded over the years such that they become more vulnerable to mortality from any given disease. In another study on whether health status in disadvantaged neighborhoods is a function of factors beyond SES, Ross and Mirowsky (2001) examined data from the 1995 Community, Crime, and Health Survey for 2,482 adults in Illinois. Comparing this data with census tract information, the researchers found that residents of disadvantaged neighborhoods generally had worse health than residents in more advantaged neighborhoods, with the effect mediated by fear of perceived neighborhood disorder.

In a study of 419 residents of 18 higher socioeconomic status neighborhoods and 235 residents of 19 lower SES neighborhoods, Steptoe and Feldman (2001) found that residential neighborhood problems function as sources of chronic stress that may increase risk of poor health. Cohen et al. (2003b) reported that although socioeconomic status is associated with premature death, other non-income community level factors such as "collective efficacy" (a measure of willingness to help out for the common good), and "broken windows" (boarded up stores and homes, litter, and graffiti) mediate the effect of socioeconomic status on premature

mortality. In another review of the literature on socioeconomic status children's health, Evans and Kantrowitz (2002) attempted to elucidate neighborhood environmental characteristics that may help to explain the socioeconomic status-health gradient. Neighborhood environmental characteristics examined included hazardous wastes and other toxins, ambient and indoor air pollutants, water quality, ambient noise, residential crowding, housing quality (e.g., adequate heat, dampness), educational facilities, work environments, and neighborhood conditions (e.g., social cohesion, perceived safety). Despite what the authors identified as significant holes in the data, they suggest data indicate that the effects of poverty or income on health are mediated by exposure to multiple environmental risk factors, with the poor (and especially the non-white poor) bearing a disproportionate burden of exposure to suboptimal, unhealthy environmental conditions in the United States.

Location – Current and Past Land Use. Research clearly indicates that rates of impaired development (as well as numerous other adverse health outcomes such as asthma) are disproportionately high in certain underserved, minority populations in urban locations (Perera et al., 2002). In addition, research has indicated that rural populations may also be at increased risk for certain exposures such as pesticides (Eskenazi et al., 1999; Wolz et al., 2003). Causative factors in observed location effects continue to be the topic of research, particularly with regard to environmental justice issues. For example, Maantay (2001) reviewed issues associated with land use planning and the influence on location of resulting environmental and health impacts. Using New York City as a case study, the authors find that noxious land uses tend to be concentrated in poor and minority areas because affluent industrial areas and those with lower minority populations are typically rezoned for other uses. For example, Meyer et al. (1999) found that children living in inner city areas of an eastern German city with a long history of mining and smelting of nonferrous ores were exposure to higher levels of arsenic in house dust compared to areas outside the city. The inner city areas were in closest proximity to the smelters and tailings piles.

As discussed previously in Section 3.2.4 on chemical exposures, neighborhood location effects on exposures to pesticides have also been the subject of considerable research. Eskenazi et al. (1999) suggest that children living in agricultural areas may be exposed to higher pesticide levels than other children because of pesticides tracked into their homes by household members, by pesticide drift, by playing in nearby fields. Lu et al. (2000) similarly found that exposure levels of children whose parents use agricultural chemicals or who live near farmland treated with pesticides were found to be significantly higher than those of other children living in the same community (Lu et al., 2000). In review a study of urban pesticide exposures, Landrigan et al. (1999) found that because pesticides are used extensively in urban schools, homes, and day care centers for urban vermin control, pesticide use in inner city areas as a key component of neurotoxic risk faced by children in theses areas also. For example, the authors report that over all counties in New York State in 1997, the heaviest use of pesticides statewide was in the urban boroughs of Manhattan and Brooklyn.

Effects of neighborhood location and past uses have also been observed with regard to exposure to potentially neurotoxic chemicals. In a study of agricultural communities, areas near old orchards with historic lead arsenate had significantly higher soil arsenic than did the other homes, and 36 percent of these homes had soil or dust arsenic levels above the minimum risk

level estimated by the Agency for Toxic Substances and Disease Registry (Wolz et al., 2003). Large areas of residential Denver have soil arsenic levels in some areas exceeding a thousand parts per million (higher than a nearby Superfund site) due to the past use of an arsenical crabgrass killer and insecticide (PAX) in the 1950s and 1960s (Folkes et al., 2001).

Ambient Air Pollution. Much of the research on ambient air pollution has been focused on respiratory health outcomes (see Sections 3.4.4 and 3.4.6), and to a limited extent on birth outcomes such as low birth weight (see Section 3.1.5). However, as discussed in Section 3.2.4 on neurotoxic effects of chemical exposures, a plethora of organic and inorganic chemicals, some of which may be components of ambient air pollution (e.g., dioxins, pesticides), have the potential to increase the risk of neurodevelopmental outcomes also. For example, Kinney et al. (2002) found that young people attending school in inner-city New York were exposed to a wide range of toxic air pollutants, such as volatile organic compounds (VOCs), aldehydes, particulate matter less than 2.5 micrometers, black carbon, and numerous particle-associated trace elements. The extent to which airborne exposures to these pollutants versus other routes of residential exposures (e.g., dust ingestion via hand-to mouth activity) contribute to neurotoxic exposures, though, is unknown. Studies have observed areas of high risk for learning disabilities to be strongly associated with air pollution facilities (Margai and Henry, 2003).

Noise and Traffic. Although it is a relatively new area of children's research, several studies regarding children's mental health, behavior, and cognitive performance in relation to noise exposures were identified in this literature search. Much of this research appears to be in relation to zones of high-intensity noise, such as around airports or major roads. In a review conducted by Stansfeld and Matheson (2003), however, the reviewers note that much of the noise-related research to date shows inconsistencies between laboratory and occupational studies and community field studies, with effects being much less pronounced in filed studies where adaptation occurs.

Haines et al. (2001a, 2001b) conducted a field study on the cognitive performance and mental health of a cohort of several hundred children aged 8-11 years attending four schools in high aircraft noise areas around London Heathrow airport. Mental health and cognitive tests were administered to the children in the schools, and salivary cortisol was measured in a subsample of children as a marker of stress. 340 children were first examined at baseline and a subset of 275 children was examined again after a period of one year at follow-up. Results at baseline indicated that, compared with children exposed to lower levels of aircraft noise, children in high noise areas had higher levels of annoyance and impaired reading comprehension, but mental health was not significantly affected (Haines et al., 2001a). At follow-up one year later, chronic aircraft noise exposure was still associated with higher levels of annoyance and perceived stress, poorer reading comprehension and sustained attention. The authors also note that adaptation to the excessive noise does not appear to be occurring in this cohort of children, based on evidence that the reading and annoyance effects were sustained over a one-year period (Haines et al., 2001b).

Other community noise research identified in this literature search reported chronically increased stress hormone levels in adult women exposed to traffic noise (Babish et al., 2001) and sleep difficulties in adults living within the flight pattern of a major airport (Bronzaft et al., 1998). In another airport noise study by Whitfield (2003), surveys of three communities around

Birmingham International Airport, UK indicated that areas of greater affluence had a significantly greater proportion of highly annoyed persons due to aircraft noise compared to more disadvantaged areas.

In contrast to the previous studies which focused on high-intensity noise, Evans et al. (2001b) examined potential health effects of every-day ambient noise exposures among 115 young children in grade four from small towns in Austria. Several indices of stress were measured in the children, including blood pressure, stress hormone (cortisol, catecholamines), heart rate, cognitive processing tests, and questionnaires on perceived stress. Results showed that children in the areas with higher ambient noise (largely from transient railroad activity) had modestly elevated resting blood pressures and overnight urinary cortisol, elevated heart rate reactivity in response to a reading test, and rated themselves higher in perceived stress symptoms on a standardized index. Girls, but not boys, also exhibited diminished motivation (i.e., increased learned helplessness behavior) in a standardized behavioral test. The authors suggest that this area of research deserves further attention, but suggest that the current study provide preliminary evidence that relatively low-intensity community noise can be associated with modest, nonauditory health effects. Lercher et al. (2002) also investigated neighborhood ambient noise exposure and mental health in children. Based on two indices of mental health (self-reporting by the child on a standard scale and rating by the teacher of classroom adjustment on a standard scale), the researchers found that exposure to ambient noise was associated with poorer classroom behavior and small decrements in children's mental health, although the correlation between mental health and ambient noise was only significant in children with additional risks, such as low birth weight and preterm birth.

Neighborhood Safety. In another study on whether health status in disadvantaged neighborhoods is a function of factors beyond SES, Ross and Mirowsky (2001) examined data from the 1995 Community, Crime, and Health Survey for 2,482 adults in Illinois. Comparing this data with census tract information, the researchers found that residents of disadvantaged neighborhoods generally had worse health than residents in more advantaged neighborhoods, with the effect mediated by fear of perceived neighborhood disorder (based on measures of crime). Aneshensel and Sucoff (1996) investigated connections between neighborhood perception of safety, SES, and mental health in a community-based sample of 877 adolescents between 12 and 17 years of age in Los Angeles County. Surveys used to collect information on mental health attributes and neighborhood perception indicated that youth in low SES neighborhoods had lower mental health ratings than those in high SES neighborhoods due to perceived dangers in their communities, such as crime, violence, drug use, and graffiti, and to a lesser extent because of perception of lack of social cohesion. Lower mental health status was characterized by symptoms of depression, anxiety, oppositional defiant disorder, and conduct disorder. Sampson et al. (1997) researched neighborhood factors related to community violence. In particular, they investigated whether collective efficacy, which is defined as social cohesion among neighbors and their willingness to intervene on behalf of the common good, is liked to reduced community violence. Results of surveys of 8,782 residents in 343 neighborhoods in Chicago, Illinois indicated that the association between violence and disadvantaged, instable neighborhoods is strongly mediated by collective efficacy.

3.2.7 References for Section 3.2

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3.3 LITERATURE ON THE RELATIONSHIPS BETWEEN HOUSING AND NEIGHBORHOOD CHARACTERISTICS AND INJURY

3.3.1 Additional Information on the Literature Review Approach for Injury

Hypothesis 3 of the National Children's Study addresses injury (see Appendix A). Of these, Hypotheses 3.1 and 3.3 potentially relate to housing or neighborhood characteristics. Specifically, Hypothesis 3.1 tests whether exposures early in life that lead to neurotoxic effects are associated with increased risk of injury, and Hypothesis 3.3 tests whether repeated head trauma has a cumulative adverse effect on neurocognitive development. Hypothesis 3.1 is currently under review by the ICC for possible strengthening.

Hypotheses 3.1 and 3.3 as currently drafted focus largely on the interactions between injury and neurotoxic exposures and neurocognitive development – these topics are also reviewed in Section 3.2 (and to some extent 3.1) of this report. The focus of this component of the literature review was therefore primarily on other housing and neighborhood risk factors associated with pediatric injuries, including head trauma, falls, burns, drowning, acute poisonings, and other physical traumas.

3.3.2 Overview

Compelling evidence exists that supports the significance of injuries, many of which are preventable, as a primary result of housing-related hazards. The National Safety Council estimates that there is one death every 16 minutes and one injury every 4 seconds in the U.S. as a result of injury events in the home (NSC, 2003). Among individuals aged 1 to 34 years, injuries are the most common cause of death (CDC/WISQARS, 2000); with the exception of motor vehicle related injury deaths, children are most commonly injured in their homes and play

environments (NSC, 2003; Dowd, 1999). In 2002, the National Safety Council estimates that home-related injuries comprised about 33% of all injury-related deaths, amounting to approximately 33,300 deaths (NSC, 2003). Although no sharp distinctions exist between injury and disease, injuries are usually defined as outcomes that occur almost immediately after contact with the causal agent.

Major categories of unintentional injuries in the home include poisoning, falls, fire and burn-related injuries, choking, drowning, suffocation, and other smaller categories such as electrocution, burns from hot liquids and steam, explosions, and excessive heat and cold. The most common types of unintentional injuries and deaths in the home, however, vary for different age groups (Agran et al., 2003). For example, as shown in Table 3.3-1, in 2000 suffocation was the leading cause of death (due to home injury) for children under four years, while the primary cause of unintentional injury-related death in the home for individuals over 75 years was falling (NSC, 2003). Table 3.3-1 provides additional detail on the numbers of deaths due to unintentional injuries in the home, by major category of injury and age group.

Table 3.3-1. Estimated [1] Number of Deaths in the U.S. Due To Unintentional Injury in the Home, By Injury Type and Age Group, 2000

Injury Type	Age group							
	0-4	5-14	15-24	25-44	45-64	65-74	75+	All Ages
Poisoning [2]	30	40	850	5,480	2,990	40	370	9,800
Falls	30	10	30	270	970	450	5,340	7,100
All other home [3]	110	70	80	290	650	450	3,150	4,800
Fires, flames and smoke	320	240	150	550	690	20	730	2,700
Choking (suffocation by ingestion)	150	20	30	160	360	290	1,090	2,100
Drowning [4]	370	80	60	130	120	130	110	1,000
Suffocation (mechanical)	470	80	60	170	140	10	70	1,000
Firearms	20	60	140	150	80	10	40	500
All home [5]	**1,500**	**600**	**1,400**	**7,200**	**6,000**	**1,400**	**10,900**	**29,000** [5]

[Adapted from NSC, 2003 and NSC, 2004 (for age specific data). Source data: CDC/NCHS (2000) National Vital Statistics System Mortality data]

[1] These values indicate National Safety Council (NSC) 2003 revised estimates based on analysis of 2000 injury data from the National Center for Health Statistics (NCHS). NSC analysis of NCHS data includes a disaggregation of home-related injuries from all other injuries using the "place of occurrence" code, or, when the "place of occurrence" code is missing, through the application of a 2-way split methodology (see NSC, 2003 Technical Appendix).

[2] Includes deaths from drugs, medicines, mushrooms, and shellfish, as well as commonly recognized poisons in solid, liquid, gas, and vapor form.

[3] Includes electrocutions, burns from hot liquids and steam, explosions, and excessive heat and cold.

[4] Although a comparison for the 2000 estimates has not yet been calculated, and comparison of NCS 1998 estimates with the 1998 NCHS National Mortality Data compiled using the WONDER database (http://wonder.cdc.gov/) suggested that previous NSC estimates for residential drowning may be low. This same disparity may also exist in the 2000 data estimates.

[5] The total estimated number of residential injury fatalities in 2000 does not include 200 deaths that occurred in motor vehicles at residences.

The risk of injury has also been shown to vary substantially by age group, as well as other factors such as race and socioeconomic status (SES). For example, although death rates for those over 75 are the highest, they also represent the smallest proportion of the population (NSC, 2003;

CDC/NCHS, 2000; U.S. Census Bureau, 2000). Nagaraja et al. investigated injury death rates for different age groups of children and adolescents (younger than 20 years of age) from 1985 to 1997, using data from the National Death Index and the U.S. Census. The authors found that the death rate due to residential injury was highest in children younger than 1 year and 1 to 4 years compared with older children. Regarding race differences, data indicates that death rates for all types of unintentional injury combined are highest for Native Americans, relative to white, Black, and Asian ethnic groups (Baker et al., 1992 (analysis of data from 1980-1986); CDC/WISQARS, 2000). The risk of injury for young children also appears to be linked to sociodemographic factors such as age and education of mother, with those of lower SES typically being at greater risk of injury (Dowswell et al., 1996; Glik et al., 1993; Santer and Stocking, 1991; Dowd, 1999; Scholer et al., 1999). For example, among children and adolescents younger than 20 years of age, Nagaraja et al. found that black children were two times more likely to die from residential injuries than white children, based on 1985-1997 data from the National Death Index. Different types of injuries may also disproportionately affect certain minority populations (USDHHS, 1990). Death rates due to residential fire for African Americans are more than twice the rate for whites (CDC/WISQARS, 2000) and in 1997, Black children ages 0 to 14 were three times as likely to die in a house fire as white children (Katcher; USDHHS, 2000). In a seven-year study of childhood falls from windows, the incidence of falls in urban areas was four times that of surrounding non-urban areas, and Black children were three times more likely to fall than non-Black children (Stone et al., 2000).

An overview of the literature found regarding injury hazards in residential environments, as well as other community factors involved in injury, is presented in Table 3.3-2 below.

Table 3.3-2. Summary of Key Literature Found on Housing/Neighborhood Characteristics Associated with Injury

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
GENERAL STUDIES AND REVIEWS		
General Housing	Death rate due to residential injury highest in children younger than 1 year and 1 to 4 years of age	Nagaraja et al.
	Individual level housing characteristics partially mediate the associations between community characteristics (e.g., concentration of poverty) and childhood injury	Shenassa et al. 2004
General Neighborhood	After adjusting for individual variability, community characteristics have an independent effect on the risk of injury in adults	Cubbin et al. 2000
	Accidental injury rates are much higher in deprived urban neighborhoods, but much of the variability can be explained by individual level characteristics	Reading et al. 1999
HYPOTHESIZED STRUCTURAL/PHYSICAL RISK FACTORS		
Housing type and age	Children have higher risk of falling from windows and balconies in older apartments built pre-1984 before building codes mandated safer distances between balcony railings; window height is also an important factor in determining falls in apartments	Istre et al. 2003
Structure, construction, condition	Many fall hazards for children are related to housing condition or structure, including: lack of safety gates or other barriers; lack of window guards or stops; lack of adequate railings; structural defects in home; insufficient lighting; tripping hazards; lack of non-slip backing on rugs and non-slip surfaces; and yard/neighborhood features such as playgrounds/trampolines	AAP 2001
Electrical system		

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Fire Related Factors	74% of average annual structure fires occur in one- and two-family dwellings/manufactured homes; 24% in apartments; kitchens are leading area of origin for home structure fires and home civilian fire injuries; cooking equipment is largest cause of fire in residential homes overall; some causes of fire differ between one- and two-family homes and apartments	Ahrens 2001b
	Lack of working smoke alarm, living in manufactured (mobile) homes, and impairment by alcohol/drugs increases the likelihood of death in cases of residential fire	Marshall et al. 1998; CDC 2003
	Living in manufactured/mobile homes (particularly those build before 1976 when building codes changed) increases likelihood of death by residential fire; residential fires most likely to be caused by heating equipment, but fatal fires most likely to be caused by smoking	Runyan et al. 1992
	Among fire-related injuries, unintentional house fires cause the most injuries; most common residential fire sources are cooking, cigarettes/lighters, electric blankets, appliances or wiring, and arson	DiGuiseppi et al. 2000
	Residential fire injury rates are highest among blacks, people aged 65 or older, and in areas with low median incomes; higher injury risk exists for fires that begin in bedrooms or living areas, fires started by heating equipment, smoking, or children playing with fire, or fires occurring in houses built before 1980; lack of functioning smoke detectors also increases risk	Istre et al. 2001
Building Materials	Investigations of the homes of children who developed lead poisoning from ingesting leaded paint chips revealed multiple housing violations requiring lead abatement	Su et al. 2002
	Among nine patients with clinically significant lead poisoning, eight children received lead exposures from lead-based paint, with seven of the cases a result of dust exposures from sanded lead paint during house renovations	Reith et al. 2003
HVAC	Backdrafting may lead to CO buildup in a home, particularly in tight homes with few sources for air to enter and high exhaust capacity (i.e., those prone to depressurization)	Nagda et al. 1996; ISU Extension Publication 1996
Moisture	Health effects associated with damp environments and related exposures include: nervous system effects; suppression of immune response; and hemorrhage in mucous membranes of the intestinal and respiratory tracts	NAS 2004
Cleanliness		
Safety devices	Approximately half of home fire deaths occur in homes without smoke alarms; homes with smoke alarms usually have a death rate from fires that is 45 to 50% lower than the rate for homes with no alarms; causes for non-functioning alarms include a disconnected power source, dead or missing battery, improper installation, or improper placement of alarm	Ahrens 2001a
	Chances of dying in a fire when home fire sprinklers are present may be one- to two-thirds lower than chances of dying in a fire in which no sprinklers are present	Conley and Fahy 1994
	Automatic fire suppression systems (i.e., sprinklers) are present in less than 1% of fires in one- and two-family homes and 7% of apartment fires, but deaths were reduced by 77% when these systems were present	Ahrens 2001b
	Use of ground fault circuit interrupters installed in household branch circuits could prevent over 2/3 of the ~300 electrocutions each year in and around the home	CPSC 2004a
	Use of GFCIs with power tools could prevent the ~ 20-30 associated electrocution deaths each year	CPSC 2004b
	49% of residential CO deaths occur when occupants are sleeping; it is estimated that approximately half of these could have been prevented if audible CO alarms were used	Yoon et al. 1998
	Swimming pool fences, pool alarms, and rigid pool covers can be successful in decreasing child pool injuries	Brenner et al. 2003
HYPOTHESIZED CHEMICAL RISK FACTORS		
Pesticides	More than 850 unique pest control products used by residents of 308 homes surveyed in Minnesota; 97% had pesticides on premises, and 88% reported using pesticides	Adgate et al. 2000
	Health care providers failed to consider pesticide poisoning as potential etiology in all of 49 cases where people were hospitalized or died after homes were sprayed in large-scale poisoning incident in Ohio	Rubin et al. 2002

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	Levels of insecticide chlorpyrifos measured indoors on day of application and the following day in some cases exceeded the No Observable Effect Level and chronic exposure Minimum Risk Level for the chemical	Fenske et al. 1990; Krieger et al. 2000
	Higher levels of pesticide exposure observed in children living in agricultural communities or near farmland compared to those living in non-agricultural neighborhoods	Lu et al. 2000; Eskenazi et al. 1999
	Risk of pesticide exposure may be amplified in urban areas, where substandard housing conditions increase chances of pest infestation	Berkowitz et al. 2003; Landrigan et al. 1999
Other organic chemicals		
Combustion by-products (CO, NO_2)	Relative risks of CO poisoning are higher among individuals living in multiunit dwellings, mobile/trailer homes, or temporary shelters than among those living in single-family homes; primary sources of poisoning are unvented combustion heating appliances and charcoal fuel	Liu et al. 2000
	Higher observed incidence of CO poisoning deaths in adults aged 45 or older may be due to pre-existing medical conditions, alcohol/drug use impairing response to CO hazards, and the fact that older people may own older products that do not conform to recent improvements in voluntary standards	CPSC 2003
	Unborn fetus is considered at increased risk for CO poisoning due to differences in fetal accumulation of CO relative to the mother	Abelsohn et al. 2002; Liu et al. 2003
	Incidence of unintentional CO poisoning, along with common sources of CO poisoning, differ across racial and ethnic categories; black and Hispanic populations have higher relative risks for CO poisoning compared to white populations	Ralston and Hampson 2000
	Major potential sources of CO (and other combustion products) include malfunctioning/inadequately vented or unvented combustion appliances, charcoal or gas grills and other devices that should not be used indoors, and the start-up or idling of vehicles in attached garages	Raub et al. 2000; Garrett et al. 1999b; EPA 2000
	While the causes of house depressurization and backdrafting are well understood, additional research is needed on the duration, frequency, and severity of depressurization-induced spillage events	Nagda et al. 1996
Lead	As age of home increases, lead concentrations in surface dust wipes also tends to increase	Pellizari et al. 1999
	Children living in pre-1950 housing are 3.9 times more likely to have elevated blood lead levels than children living in post-1977 housing; no differences in risk observed between children living in a 1950-1977 home versus a post-1977 home	Roberts et al. 2003
	No significant differences observed between children's blood lead levels in public housing developments and those in non-development housing after controlling for housing age	Rabito et al. 2003
	Highest risks of lead exposure are for impoverished children who live in older, poorly maintained rental housing (esp. in northeastern and midwestern U.S.), as well as more affluent children who live in older housing (esp. when under renovation)	Lanphear et al. 2003
Asbestos, fiberglass		
Other inorganic chemicals	Nearly half (48%) of unintentional poisoning deaths reported in 2000 were attributable to narcotic and hallucinogenic drugs	NSC 2003
Also see "Ambient air pollution" and "Traffic" under External Factors Affecting Housing		
HYPOTHESIZED BIOLOGICAL RISK FACTORS		
Multiple allergens		
Dust mites		
Cockroaches		
Other insects (ticks, fleas, mosquitoes)		
Mice Rats	All Hantaviruses known to cause Hantavirus Pulmonary Syndrome are carried by the New World rats and mice in the *Sigmodontinae* family, including at least 430 species of mice and rats throughout North and South America	CDC 2002

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Molds	Health effects beyond respiratory symptoms that have been researched in relation to damp environments or exposures resulting from damp environments (e.g., molds or bacteria) include nervous system effects, suppression of immune response, and hemorrhage in mucous membranes of the intestinal and respiratory tracts	NAS 2004
Pets		
Bacteria, endotoxins, /microbial VOCs		
Other triggers (e.g., viral agents, parasites)		
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS		
Location	86% of falls reported over a 7-year period were from windows; children 0-4 years of age had a higher rate of falls than children aged 5-14; prevalence of falls in urban area was four times that of surrounding non-urban area	Stone et al. 2000
	Approximately 103 farm fatalities and over 30,000 nonfatal injuries occur annually in youth under age 20 working or living on U.S. farms; although children working in agriculture make up only 8% of the population of working minors, they account for up to 40% of work-related fatalities	Perry 2003
	Residential fires and fire deaths differ by community size, with rural areas having the highest fire death rates	Ahrens 2001b
Zoning/building codes		
Ambient air pollution		
Traffic	Urban sprawl has a significant effect on traffic and pedestrian fatalities, with every 1% increase in the index (i.e., more compact, less sprawl) associated with a 1.47 to 3.56% reduction in pedestrian fatality rates	Ewing et al. 2003a
	Although most child pedestrian and bicyclist injuries occurred on residential streets, the risk of injury was greater on larger boulevards and tended to cluster by region within the city; sites where accidents generally occurred had a larger proportion of traffic exceeding posted speed limits and were four times more likely to be near a convenience store, gas station, or fast food store	Kraus et al. 1996
	Although areas with busier streets (greater posted vehicle speeds and/or greater traffic volumes) were associated with increased risk for pedestrian injuries, the lack of pedestrian crossing devices, crosswalks, or sidewalks was not associated with an increased risk	Mueller et al. 1990
	Child pedestrian injury rates were positively correlated with the number of streets crossed (exposure to traffic), and the number of streets a child had to cross was inversely related to SES	Macpherson et al. 1998
	Speed humps were associated with a reduced risk of children being injured within their neighborhood and being struck by a car in front of their home	Tester et al. 2004
Noise		
Crime rates, violence, neighborhood safety		
Recreational facilities, playground equipment	No serious head injuries occurred in municipal playgrounds over five years of injury surveillance after safety surfaces were installed	Norton et al. 2004
	Annual injury rate for 16 schools and 16 parks observed was low overall: 0.59 injuries per 100,000 uses of equipment in schools and 0.26 per 100,000 uses of equipment in parks; annual number of injuries per standardized number of uses could be used to determine the relative risk of particular pieces of playground equipment	Nixon et al. 2003
	Annual incidence of playground injuries was 7 in 1000 among boys and 4 in 1000 among girls, with a 2.2 times higher risk of injury in public than in private playgrounds; children in public playgrounds had eight times higher odds for concussion and six times higher for open wounds relative to children at private playgrounds	Petridou et al. 2002
Pedestrian and bicycle access	*See "Traffic" row*	
Water hazards	Majority of drownings occur in a natural body of water for all age groups, though most drownings among children aged 0-4 years occur in residential swimming pools, with the child typically gaining access to pool via inadequate fencing, an open or ineffective gate, or a ladder left in the down position	Browne et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
	Lack of swimming safety devices (e.g., pool fences, pool alarms) is a major risk factor in child pool injuries	Brenner et al. 2003
HYPOTHESIZED BEHAVIORAL & SES RISK FACTORS		
SES mediators	Incidence of falls from urban areas is four times that of surrounding non-urban areas; black children are three times more likely to fall than non-black children	Stone et al. 2000
	Groups at increased risk of fire-related injuries and death include children 4 years and under, African-Americans and Native Americans, poor Americans, persons in rural areas, and those living in manufactured homes or substandard housing	CDC 2003
	Higher rates of injury deaths caused by fires for minorities is consistent with higher overall rates of home-related injuries associated with poverty/low levels of education (e.g., due to substandard housing or lack of building code enforcement)	Schwarz et al. 1993; USDHHS 1990
	SES factors such as proportion of low-income households, single-parent families, non-high school graduates, and unemployment are all significant predictors of risk for both unintentional and intentional injury; single most important predictor is low income	Durkin et al. 1994
	Community characteristics, including SES, have an independent effect on the risk of injury	Cubbin et al. 2000
	Although a higher SES has a strong inverse association with risk of fatal injuries, the relationship between SES and nonfatal injuries is less consistent	Cubbin and Smith 2002
	Within three low-income communities, variations in neighborhood characteristics influenced injury prevalence rates; higher rates of housing violations in the neighborhood were associated with increased risk of injury in children under five years of age	O'Campo et al. 2000
	SES status, while associated with mortality, does not fully explain health disparities	Cohen et al. 2003
Other behavioral factors		

As shown in Table 3.3-2, literature regarding injury outcomes was found on a variety of different housing and neighborhood factors. Generally, the linkages between hazards in the home and major housing-related injuries, including burns and other fire-related injuries, falls, drowning, and poisoning are well established. The following sections detail the literature found on specific housing and neighborhood related risk factors for childhood injuries.

3.3.3 Structural/Physical Attributes of Housing/Neighborhoods Associated with Injury

Housing Type and Age. The effects of home age and type on injury have been investigated in several studies identified in the literature, primarily in relation to lead based paint poisoning.

Lead-based Paint in Older Homes. As also discussed in Section 3.2.4 of this report (neurotoxic effects), the reviews identified in this literature search generally support the finding that home age is generally more important that housing type when assessing lead based paint hazards. Pellizari et al. (1999) investigated the relationship between age of housing and levels of lead in dust in the home using data collected as part of the Nation Human Exposure Assessment Survey (NHEXAS) in the Great Lakes region. Analysis of the NHEXAS data showed that as the age of the home increased, lead concentrations in surface dust wipes also tended to increase, with a mean dust lead concentration of 128 µg/g in homes built since 1980 and 1075 µg/g in homes built before 1940. Utilizing geographic information system (GIS) techniques, Roberts et al. (2003) assessed the relationship between risk of elevated blood lead level (BLL) and age of housing in Charleston County, South Carolina. In the county, 1,044 cases of elevated BLL were found, and 20 percent of children living in pre-1950 homes had

elevated BLLs. Results of the analysis also showed that children living in pre-1950 housing were 3.9 times more likely to have an elevated BLL than children living in post-1977 housing, although no differences in risk were observed for children living in a 1950-1977 home versus a post-1977 home. It was also noted in the study that a large number of elevated BLLs were also found in an area of newer houses, but near a potential point source, suggesting that GIS techniques can be useful in identifying areas of unexpected risk clustering from potential point sources. Rabito et al. (2003) conducted a case-control study among 7,121 children between the ages of 6 months to 71 months to assess the risk of an elevated BLL among high-risk children in public housing in New Orleans, and to determine the efficacy of federal lead regulations designed to specifically protect children in public housing developments. Although elevated BLLs were found in 29% of the children, no significant differences were observed between children's BLLs in public housing developments and those in nondevelopment housing after controlling for housing age. These findings were supported in a recent review by Lanphear et al. (2003), who noted that the highest risks of lead exposure are for impoverished children who live in older, poorly maintained rental housing (especially those who live in the northeastern and Midwestern regions of the U.S.), as well as more affluent children who live in older housing (especially housing undergoing renovation). The overall prevalence of housing units in the U.S. that contain lead-based paint was investigated in the National Survey of Lead and Allergens in Housing, discussed in see section 3.2.4 under "lead" (Jacobs et al., 2002).

Carbon Monoxide Poisoning and Housing Type. In addition to literature on lead exposures and housing type and age, one study was also found that investigated risk factors for carbon monoxide poisoning associated with housing type. Liu et al. (2000) analyzed data on 270 non-vehicular carbon monoxide poisoning fatalities that occurred between 1979 and 1988 in California. The data indicated that relative risks of carbon monoxide poisoning were higher among individuals who lived in multiunit dwellings, dwelled in mobile/trailer homes, or resided in temporary shelters, than among individuals who lived in single-family homes.

Falls and Housing Age. Finally, in a study on falls and housing structure (also see discussion below), Istre et al. (2003) found that children had a higher risk of falling from windows and balconies in older apartments (i.e., built before 1984) built before building codes mandated safer distances between balcony railings. The older apartments also tended to have windows that were closer to the floor and more accessible to children.

Housing Condition and Structure. Studies identified in this literature search that examined housing conditions and structural attributes in relation to injury outcomes focused primarily on falls. Specific literature on the incidence of head traumas as an outcome of housing-related falls (see NCS Hypothesis 3.3), however, was not identified in this literature search.

Falls and Housing Condition and Structure. One of the major types of injury associated with certain housing conditions and structural conditions is falls (AAP, 2001). In 2000, falls were the leading cause of nonfatal injuries for all age groups except those 15-34 years old (CDC/WISQARS, 2000). Although falls are an infrequent cause of death during childhood, falls are a major cause of nonfatal injury in children (NSC, 2003). Each year, more than 3 million children are treated in emergency departments for injuries from falls (although not limited to home falls), with more than 40% occurring among infants, toddlers, and preschoolers (CDC,

2000a). In residential settings, many fall hazards for children (beyond lack of child supervision) are related to housing condition or structure, including: lack of safety gates or other barriers to block stairways and other areas dangerous for children play (e.g., fire escapes, high porches, balconies); lack of window guards or stops for windows accessible to children; lack of adequate stair and balcony railings; structural defects in the home (e.g., uneven floors); insufficient lighting on stairs and in other areas; tripping hazards such as toys and objects on the floor or stairs; lack of non-slip backing on rugs and other unsecured flooring; lack of non-slip surfaces in the bathroom; and yard and neighborhood features such as playgrounds and trampolines (AAP, 2001).

Istre et al. (2003) investigated in further depth the specific circumstances surrounding children's falls from balconies and windows. Through interviews with parents and measurements of windows and balcony rails in some cases, the study collected detailed information on 98 children treated for fall injuries (falls from buildings only) in Dallas County, Texas from 1997 to 1999. Data showed that 77 percent of the falls involved apartments, and of these, 52 percent were from windows, 45 percent from balconies, and 3 percent from unknown sites. Many of the apartments were older apartments built before 1984. Additional data on apartment characteristics indicated that the distance between balcony rails and window height were two important factors in determining falls in apartments. For example, in more than two thirds of the falls from balconies, the child fell from between the balcony rails, all of which were spaced more than 4 inches apart and found in apartments built before 1984. In more than two thirds of the falls from windows, the window was positioned within 2 feet of the floor. The authors of the study note that in many cases, current building codes do not apply to older apartments, where most of these falls occurred.

Fire and Burn Hazards. Roughly eight out of ten fire deaths in the U.S. occur in the home (Hall, 1997). Smoke inhalation accounts for the largest percent of home fire injuries overall; about half of all victims are asleep when the fire occurs (Hall, 1997). A Consumer Products Safety Commission (CPSC) study of fires associated with consumer products (e.g., cooking equipment, heating equipment, electric and gas-fueled ranges and ovens) found that residential fires accounted for about 75 percent of all structure fires in 1998 and resulted in 90 percent of civilian deaths (CPSC, 2001a). Based on an analysis of 1994-1998 national data, The National Fire Protection Association also reported that 74 percent of the annual average of 418,500 structure fires occurred in one- and two-family dwellings or manufactured homes, and 24 percent were in apartments (Ahrens, 2001b).

Origins, Causes, and Risk Factors for Home Fires. The National Fire Protection Association reports that kitchens are the leading area of origin for home structure fires and for home civilian fire injuries, based on 1994-1998 national annual averages (Ahrens, 2001b). Almost half of all apartment fires and one-quarter of the fires in one- and two-family homes started in kitchens, with bedrooms ranking second, and living rooms, family rooms or dens ranking third. Fires in chimneys ranked fourth in frequency, although they were a much larger problem in one- and two-family homes compared to apartments.

From 1994-1998 the largest cause of residential fires in residential homes overall (including one and two-family homes, manufactured homes, and apartments) was cooking equipment (22.6%),

followed by heating equipment (including central systems and portable heaters), (14.5 %); suspicious or incendiary fires (12.1 %); other equipment (e.g., electronics) (10.5%); electrical distribution (9.4%); appliances, tools, and air conditioning (7.2); smoking materials (5.2); open flame, torches, or embers (4.8); and children playing with matches or lighters (4.5%). However, the data indicate that the causes of home fires differ in one and two family homes vs. apartments. For example, cooking equipment was the cause of 18.8 percent of fires in one and two family dwellings and manufactured housing, followed closely by heating equipment (17.5 percent). In contrast, for apartments, cooking equipment was the cause of 36.6 percent of fires and heating equipment was only involved in 5 percent of apartment fires. Systems that are centrally installed and maintained in apartment building tend to account for a lower proportion of fires than they do in family homes (Ahrens, 2001b).

Lack of a working smoke alarm, living in manufactured (mobile) homes (particularly those built before 1976 when building codes changed (Runyan et al., 1992), and impairment by alcohol or drugs also increase the likelihood of death in cases of residential fire (Marshall et al., 1998; Runyan et al., 1992; CDC, 2003). According to data from the National Center for Injury Prevention and Control and National Fire Protection Association, approximately half of home fire deaths occur in homes without smoke alarms (Ahrens, 2001a). Alcohol is involved in approximately 40 percent of deaths associated with residential fires (Runyan et al., 1992).

Groups at increased risk of fire-related injuries and deaths include children 4 years and under, African-Americans, and Native Americans, poor Americans, persons in rural areas, and those living in manufactured homes or substandard housing (CDC, 2003). The National Safety Council reports that relative to the rest of the population, death rates due to fire are highest among children ages 0 to 4 and individuals over age 75 (NSC, 2000). Young children and the elderly may have difficulty escaping from burning buildings, even in cases where a smoke alarm may be sounding. Death rates relative to the entire population are also higher for certain minority populations. For example, African Americans and Native Americans die at more than twice the rate of whites from residential fires (USDHHS, 2000). The higher rates of injury deaths caused by fires for minorities is consistent with the higher overall rates of home-related injuries associated with poverty or lower levels of education (e.g., due to substandard housing and lack of building code enforcement) (Schwarz et al., 1993; USDHHS, 1990).

Relative Risk of Fire-Related Hazards. In overview, the primary residential hazards associated with burns and fire-related injuries in the literature are:

- Lack of functional smoke alarms near or inside bedrooms and on every floor of the house,
- Lack of fire extinguishers,
- Lack of Arc Fault Circuit Interrupters (AFCIs)
- Lack of anti-scald devices for shower heads and faucets,
- Lack of safety plug covers to prevent electric burns, and
- Behavior (e.g., water heater thermostats set above 120 F; smoking inside the home; not establishing and practicing fire escape routes and procedures; not preventing children's access to matches and lighters; leaving burning candles unattended; storing flammable

liquids under unsafe conditions; not turning pot handles to back of the stove and leaving hot foods and liquids near the edges of tables or counters; and not testing bath water).

Several studies identified in this literature search attempted to examine the relative risks of various fire-related hazards in homes in the context of community or other (e.g., SES) risk factors. DiGuiseppi et al. (2000) investigated the prevalence of non-fatal injuries from residential fires by analyzing data from emergency departments, hospitals, ambulance services, the fire department, the health department, and local coroner records in a racially diverse, dense urban area of low socioeconomic status in London between 1996 and 1997. Of 131 fire related injuries, unintentional house fires caused the most injuries (63 percent). The most common residential fire sources were cooking (31 percent), cigarettes or lighters (18 percent), electric blankets, appliances or wiring (8 percent), and arson (8 percent). Istre et al. (2001) also examined specific residential or neighborhood factors related to house fires and injury rates in an analysis of fire department, ambulance, hospital, and coroner reports in Dallas, Texas from 1991 through 1997. Of 223 injuries reported (91 fatal and 132 nonfatal) from 7,190 house fires, injury rates were highest among blacks, people aged 65 or older, and in census tracts with low median incomes (apartment and mobile home fires were excluded in this study). Within the house, the risk of injury was higher for fires that began in bedrooms or living areas; that were started by heating equipment, smoking, or children playing with fire; or that occurred in houses built before 1980. Injuries also occurred more often in houses without functioning smoke detectors, which were most commonly lacking in houses in neighborhoods with the lowest median incomes. Runyan et al. (1992) studied the causes of 151 fatal residential fires (compared to a control set of nonfatal fires) in single-family dwellings in predominantly rural areas of North Carolina over a 13-month period. Overall residential fires were most likely to be caused by heating equipment, but fatal fires were more likely to have been caused by smoking. Other factors that were associated with a higher risk of fire death included residence in a mobile home and the absence of a smoke detector, although the presence of an alcohol-impaired person was the strongest independent risk factor for death in the case of a fire.

Burns/Scalds. Burns also commonly occur in residential settings from contact with hot foods and liquids (scalds), objects, or electricity. In 1997, an estimated 12,400 scald burns were sustained by children, nearly a quarter of which were caused by hot tap water (Schieber et al., 2000). Most scald burns occur as a result of contact with hot food and drink or tap water, and most deaths related to scalds occur primarily in children younger than 4 years old (NSKC, 2001). Burns as a result of scalding by hot tap water are generally more severe than other scalds, and occur most frequently in the bathtub or shower, but may also occur in the kitchen or bathroom sink. Most victims of scald burns from tap water are younger than 5 years, although other high-risk groups include the elderly and those with physical or mental disabilities.

Building Materials. Several studies were identified in this literature search that linked building materials used in residential environments with chemical exposures, including some chemical exposures that could potentially result in injury. Most notably, this includes fatal exposure to lead based paint used in older housing stock (CDC, 2001; Su et al., 2002), which is discussed below in Section 3.3.4. Other building materials were also associated with chemicals exposures in the literature (e.g., treated wood with preservatives containing arsenic), although the extent to which these materials may result in acute exposures causing immediate injury is

unknown. Much of the literature regarding chemical exposures associated with building materials, including that on lead based paint, is focused on neurotoxic outcomes and is discussed in Section 3.2 of this report.

Heating, Ventilation, and Air Conditioning (HVAC) Systems. In buildings, ventilation system characteristics often influence indoor air quality. This may include concentrations of indoor air toxics that could possibly lead to injury, including carbon monoxide (CO) and other combustion appliance gases. For example, air exchange rate, building volume, and air mixing within the indoor compartments have been shown in the literature to affect carbon monoxide concentrations in the indoor environment (EPA, 2000). Adequate ventilation and a supply of fresh air is important to help carry CO and other combustion pollutants up the chimney, stovepipe, or flue, and is necessary for the complete combustion of any fuel (CMHC, 1998; ISU Extension Publication, 1996). Another potentially HVAC-related problem that may lead to CO build up in a home is backdrafting, particularly in tight homes with few sources for air to enter and high exhaust capacity that are prone to depressurization (Nagda et al., 1996; ISU Extension Publication, 1996). Additional information on CO poisoning and housing factors that may lead to elevated CO levels in homes is provided in Section 3.3.4 of this review.

Moisture. As discussed in Section 3.2.5 of this review (neurodevelopmental effects), other health effects beyond respiratory symptoms have been researched in relation to damp environments including nervous system effects, suppression of the immune response, and hemorrhage in the mucous membranes of the intestinal and respiratory tracts (NAS, 2004).

Safety Devices. Many types of safety devices are available to prevent injuries in the home, including devices to prevent falls, fires, burns, electrocution, carbon monoxide poisoning, and drowning.

Fall Prevention. As discussed above, lack of safety devices are often associated with children's falls in the home. Safety devices used in the home to prevent falls include safety gates to block stairways and other areas dangerous for children, window guards or stops for windows accessible to children, non-slip backing on rugs and other unsecured flooring, and non-slip surfaces in the bathroom (AAP, 2001).

Fire and Burn Prevention. Many devices can be used to prevent burns and deaths associated with fire. These include: smoke alarms, fire extinguishers, home sprinklers, escape ladders, anti-scald devices for showers and sinks, safety covers for outlets, and arc fault circuit interrupters (AFCIs).

The presence of a functioning smoke alarm has proven to be effective in reducing mortality from residential fires (Dowd, 1999; Ahrens, 2001a; Ahrens, 2001b). According to the National Fire Protection Association (NFPA), homes with smoke alarms usually have a death rate from fires that is 45 to 50% lower than the rate for homes that have no alarms (Ahrens, 2001a). As of 1997, 94 percent of U.S. homes had at least one smoke alarm, although apartments were more likely to have these devices than one- and two-family homes (Ahrens, 2001b). On average, half of the home fire deaths occur in the 6% of homes with no smoke alarms (Ahrens, 2001a). In addition, the NFPA reports that half of the deaths from fires in homes equipped with smoke

alarms resulted from fires in which the smoke alarm did not sound. According to the U.S. Consumer Product Safety Commission (as cited in NSC, 2000), of homes containing at least one smoke alarm, one of every five has no functioning alarm. Causes for non-functioning smoke alarms include: a disconnected power source, a dead or missing battery, improper installation, or improper placement of the alarm (Ahrens, 2001a). The effectiveness of smoke alarms is also influenced by their number and placement in the home. At least one smoke alarm should be installed on every floor of the home, including the basement, and outside each sleeping area. Because smoke rises, alarms should be mounted high on walls or ceilings, away from windows, doors, or forced-air registers where drafts could interfere with their operation.

Home fire sprinklers can also be used as an effective strategy for preventing deaths in house fires. Fire sprinklers can effectively extinguish residential fires and save lives without human action. This protection is especially beneficial for those who cannot escape easily without help, such as children, the elderly, the disabled, or intoxicated persons. Conley and Fahy (1994) estimate that the chances of dying in a fire when sprinklers are present may be one- to two-thirds lower than the chances of dying in a fire in which sprinklers are not present. Kay and Baker (2000) estimate that while smoke alarms can reduce the fire death rate by 50%, sprinklers alone can reduce deaths by about 70%, and the combination by 80%. The NFPA reports that on average (annual averages 1994-1998) automatic fire suppression systems (i.e., sprinklers) were present in less than 1 percent of fires in one- and two-family homes and in only 7 percent of the apartment fires, but deaths were reduced by 77% when these systems were present (Ahrens, 2001b)

As of the late 1980s, water heater manufacturers have voluntarily agreed to preset all electric water-heater thermometers to 120°F (Dowd, 1999). However, because thermostats in water heaters can sometimes be inaccurate (especially in the case of older water heaters), parents are advised to measure hot water temperatures using a thermometer, and if necessary, lower the temperature so that it does not exceed 125°F to 130°F, where the likelihood of scald injury increases (Dowd, 1999; Schieber et al., 2000). However, residents of apartments may not have access to or control of their hot water settings (Doc4Kids Project, 1998).

CPSC reports that arc fault circuit interrupters (AFCI) can provide added protection from electrical fires. AFCIs work by responding to early arcing and sparking conditions in home wiring to prohibit or reduce potential electrical fires from happening. The National Electrical Code, a widely-adopted model code for electrical wiring, has required AFCIs for bedroom circuits in all new residential construction since January 2002.

Electrocution Prevention. The use of ground fault circuit interrupters (GFCI) installed in household branch circuits could prevent over two-thirds of the approximately 300 electrocutions each year in and around the home (CPSC, 2004a). Installation of this device could also prevent thousands of burns and electric shock injuries each year. Electrocutions occur when electrical current escapes from an appliance and travels through the victim to the ground (e.g., when a person comes into contact with an electrical appliance while touching a grounded metal object or while submerged in water). If the GFCI senses any disruption in current, it turns off power to the affected circuit and prevents delivery of a lethal dose of electricity (CPSC, 2004a). Local building codes generally require the installation of GFCIs in rooms with water sources, such as kitchens and bathrooms. The use of GFCIs with power tools could prevent the approximately

20-30 associated electrocution deaths each year (CPSC, 2004b). CPSC also recommends the use of GFCIs for protection against hazards involving electrical circuits and underwater lighting circuits in and around pools, spas, and hot tubs (CPSC, 2004b).

Carbon Monoxide Alarms. Along with regular inspection of combustion appliances, properly working CO alarms can provide home occupants with an early warning before indoor CO levels reach dangerous levels. For example, in a study of unintentional CO poisoning deaths in New Mexico (1980 through 1995), Yoon et al. (1998) found that 49% of residential CO deaths occurred when the occupants were sleeping, and estimated that (of the victims without the presence of alcohol in their blood) approximately half (78) of the deaths could have been prevented if audible CO alarms were used. Research by the Home Safety Council President indicates that only 35 percent of American homeowners had a carbon monoxide detector in their home (Home Safety Council, 2003).

CPSC believes that CO alarms are as important to home safety as smoke alarms, and recommends that homes have at least one carbon monoxide alarm on each sleeping floor (preferably every floor), with an additional alarm in the area of any major gas burning appliances. CPSC currently considers any alarm that conforms to the most recent Underwriters Laboratories standard (UL 2034) or the International Approval Services Standard IAS 6-96 acceptable for added protection against CO poisoning in the home, to be used in conjunction with proper use and upkeep of appliances that can produce CO. CO alarms should be installed according to the manufacturer's instructions (e.g., alarms should not be covered by furniture or draperies).

Safety Devices for Swimming Pools. According to the CPSC, 60% fewer drownings occur in in-ground pools with four-sided isolation fencing as in-ground pools without four-sided fencing (CDC, 2000b). The use of non-rigid pool covers in some cases is believed to have contributed to drownings, but the CPSC reports that properly secured, rigid safety covers on spas can reduce drownings, as can the use of power safety covers on pools when not in use (CPSC, 2002a; CPSC, 2003b). Similarly, in a review of the literature on prevention of drowning deaths and water-related injuries in children, Brenner et al. (2003) found evidence that swimming pool fences, pool alarms, and rigid pool covers can all be successful in decreasing child pool injuries. Studies included in the review showed that 4-sided fencing isolating a pool from the house and the yard can decrease the number of pool immersion injuries among young children by more than 50%. Adequate fencing was described as being at least four feet high, and with no openings under the fence or between uprights exceeding four inches. Detailed guidelines for safety barriers for home pools are available online from the CPSC at www.cpsc.gov/CPSCPUB/PUBS/Pool.pdf

3.3.4 Chemical Attributes of Housing/Neighborhoods Associated with Injury

In the context of residential injuries, discussion of chemical exposures in this section is primarily focused on those that would result in acute health effects. Discussion of lead poisoning, although not always acute in nature, is also included here due to its importance in residential environments. Non-fatal residential lead exposures, as well as other chronic chemical exposures in homes that may result in non-acute health outcomes (e.g., neurodevelopmental effects, respiratory symptoms), are discussed in other sections of this paper (See Section 3.2 on

neurodevelopmental/cognitive effects, Section 3.1 on adverse pregnancy outcomes, and Section 3.4 on respiratory health).

Exposure to toxic substances is common among the pediatric population, though the death rate due to this exposure is generally low for this age group (Dowd, 1999; also see Table 3.3-2). The majority of deaths due to poisoning occur in middle-aged adults (see Table 3-3.2). In 2002, the American Association of Poison Control Centers documented 727,036 cases of nonpharmaceutical pediatric (<6 years of age) poisonings in the United States (Watson at al., 2003). Ninety-two percent of all of the exposures reported in 2002 occurred in the home.

In indoor environments, potentially toxic substances may be present as solids, liquids, gases, or airborne particulates. Common causes of unintentional poisonings include drugs, carbon monoxide, cleaning products, solvents, plants, and agricultural pesticides and herbicides. Nearly half (48%) of the unintentional poisoning deaths reported in 2000 were attributable to narcotic and hallucinogenic (including many illegal) drugs (NSC, 2003). The most common cause of poisoning by gases and vapors is carbon monoxide (CO) (NSC, 2001). Lead poisoning is an important concern that disproportionately affects children, nonwhites, and the poor (EPA, 1998).

The primary residential hazards associated with unintentional poisonings are:

- Behavior (e.g., not locking up dangerous substances, improper use of products, not opening garage door when warming car, accidental or improper drug ingestion),
- Exposure to lead-based paint (e.g., dust from sanding lead-based paint, peeling paint chips),
- Lack of child-proof storage for toxic substances,
- Lack of proper ventilation and professional inspection and maintenance of furnaces, fireplaces, wood-burning stoves, and gas appliances, and
- Lack of carbon monoxide alarms.

Pesticides. Cases of poisoning resulting from accidental acute exposure to pesticides have been well-documented in children. Other non-fatal effects of pesticide exposure that have been suggested in the literature, including neurodevelopmental effects and potential asthma exacerbation, are discussed in Section 3.2.4 and 3.4.4 of this report, respectively.

Highlighting the magnitude of potential home pesticide exposures, in-home interviews and inventories conducted of 308 homes in Minnesota as part of the National Human Exposure Assessment Survey (NHEXAS) indicated that more than 850 unique pest control products were being used. 97% of the homes had pesticides on the premises and 88% of households reported the use of pesticides (Adgate et al., 2000).

Of the 727,036 cases of nonpharmaceutical pediatric (<6 years of age) poisonings documented in the U.S. in 2002 by the American Association of Poison Control Centers, 7% (50,415) were attributable to pesticide exposures, although this may actually be an underestimate of the true number of cases each year due misdiagnosis – the symptoms between mild pesticide poisoning and the "flu" or other common ailments are often very similar. For example, in an investigation of a large-scale poisoning incident involving methyl parathion that was illegally applied in Lorain County, Ohio homes over the course of 5-7 years, Rubin et al. (2002) observed that health

care providers failed to consider pesticide poisoning as a potential etiology in all of the 49 cases where people were hospitalized or died after their homes were sprayed. The symptoms of pesticide poisoning include headache, fatigue, dizziness, shortness of breath, and loss of appetite with nausea, vomiting, stomach cramps, and diarrhea (University of Nebraska Cooperative Extension, 1997). For very young children, the increased salivation, crankiness and loss of appetite due to mild pesticide poisoning may be often dismissed as "teething."

Cases of acute poisoning are generally due to direct contact with a product via inadvertent ingestion, dermal contact, and/or inhalation. Since 1981, the Federal Insecticide, Fungicide, and Rodenticide Act (FIRFRA) has mandated child-resistant packaging for all highly toxic pesticides (including disinfectants) sold for residential use in the U.S. (Spann et al., 2000). The majority of sub-acute poisoning cases (i.e., "mild poisoning" cases with flu-like symptoms) occur after indoor use of insecticides, such as in homes or schools, and appear to be primarily due to either misapplication or a failure to fully ventilate the rooms after application. In two studies examining such scenarios, levels of the insecticide chlorpyrifos were measured indoors on the day of application and the following day, and these data were combined with assumptions about exposure to estimate a dose for comparison with the NOEL (No Observable Effect Level; 30 μg/kg/day for chlorpyrifos) and the recently defined chronic exposure MRL (Minimum Risk Level; 1 μg/kg/d for chlorpyrifos) reported by the Agency for Toxic Substances and Disease Registry (ATSDR) (Fenske et al., 1990; Krieger et al., 2000; ATSDR, 2000). Both studies found that the NOEL and chronic exposure MRL were in some instances exceeded in the short term.

In the event of acute or sub-acute poisonings, the causative event or product can usually be inferred by parents or caregivers via area surveillance. Because "mild poisonings" (e.g., with flu-like symptoms) often occur when a pesticide misapplication is made in the home or school, sudden onset of conditions for multiple individuals can be used as an indication of possible sub-acute exposure.

Housing characteristics that can create pesticide exposure risks include aspects of the housing condition, such as a degraded foundation and housing structure which allow pest migration into the home, multifamily or conjoined housing in which infestation in one unit allows migration of pests to the adjoining units, lack of proper/safe food storage which attracts pests, and poor ventilation which does not allow the pesticide residue to dissipate after an application (Health Canada, 2001; Alliance for Healthy Homes, 2003).

Neighborhood factors (e.g., rural/urban location) can also influence pesticide exposure risk. Higher levels of pesticide exposure have been observed in children living in agricultural communities or near farmland compared to those living in non-agricultural neighborhoods (Lu et al., 2000; Eskenazi et al., 1999). However, risk of pesticide exposure may also be amplified in urban areas, where substandard housing conditions increase the chances of pest infestation and, consequently, pesticide usage (Berkowitz et al., 2003; Landrigan et al., 1999).

Carbon Monoxide and Other Combustion By-products. Carbon monoxide poisoning is the most common cause of acute poisoning by inhaled gases in residential situations (NSC, 2000). As noted previously (see Section 3.2.4 on neurological effects), carbon monoxide (CO) is

a poisonous gas produced as a combustion by-product. CO interferes with oxygen transport to the tissues and organs of the body and leads to adverse health effects, particularly in sensitive organs such as the brain and heart. The onset and severity of CO poisoning symptoms is influenced by the level and duration of reduced oxygen availability (hypoxia), as well as the sensitivity of the individual. It is possible for permanent injury, with resulting disability, to occur from a single, acute CO exposure. Individuals who suffer exposures to elevated levels of CO may be unaware of the source of their health problems because CO poisoning, both chronic and acute, can cause symptoms that are varied and mimic illnesses like the flu and other bacterial and viral infections. Symptoms of exposure can begin with a slight headache, subtle sensory-motor deficits, nausea, vomiting, impaired vision, fatigue, dizziness, and shortness of breath. If exposures continue, symptoms become more intense, progressing to a loss of consciousness. Eventually, at high enough levels, CO causes death by asphyxiation. Survivors of CO poisoning may also have long-term neurological effects, as discussed previously.

Although fatal exposures to CO appear to be declining since the 1980's, there are still hundreds of deaths per year in the U.S. from CO, with many of these deaths occurring at home (CPSC, 2003a). According to the U.S. CPSC, in 1999-2000, the total number of unintentional CO poisoning deaths associated with consumer products (e.g., household appliances), excluding those associated with fire or motor vehicles, averaged about 124 annually (CPSC, 2003a). The majority (64%) of these deaths occurred in the home. Beyond CO fatalities associated with consumer products, many additional deaths occur each year as a result of CO poisoning from motor vehicle exhaust, including some deaths in homes from motor-vehicle exhaust infiltration into the living space from an attached garage.

In addition to CO poisoning fatalities, it is estimated that thousands more go to hospital emergency rooms for treatment of non-fatal CO poisoning each year (Hampson, 2000). CPSC estimates that in 1998, 7,700 people were treated in U.S. hospital emergency departments for suspected non-fire, non-motor vehicle CO poisonings (CPSC, 1999).

Other Risk Factors. Adults tend to comprise the majority of the deaths occurring from CO poisoning. For example, from 1999-2000, adults 45 years and older accounted for 56 percent of deaths, while children less than 15 years of age only accounted for an average of five percent of yearly CO poisoning deaths (CPSC, 2003a). CPSC suggests that several factors may contribute to the higher observed incidence of CO-poisoning deaths in older adults, including pre-existing medical conditions that lower a victim's tolerance to CO in the bloodstream, alcohol and recreational drug use impairing response to CO hazards, and the fact that older age groups may tend to own older products that do not conform to more recent improvements in voluntary standards (CPSC, 2003a). However, it should also be noted that the unborn fetus is also considered at increased risk from CO poisoning due to differences in fetal accumulation of CO relative to the mother (i.e., CO levels may be much higher in the fetus) (Abelsohn, et al., 2002; Liu et al., 2003)

Ralston and Hampson (2000) found that the incidence of unintentional CO poisoning differs across racial and ethnic categories. Among 586 Washington state residents treated for severe CO poisoning from 1987 to 1997, black and Hispanic populations had higher relative risks for CO poisoning than white populations (home and non-home CO poisonings included). In addition,

the most common sources of CO poisoning differed by racial/ethnic category. For example, for Hispanic and black populations, about 67% and 40%, respectively, of poisonings were due to indoor burning of charcoal briquettes, while all boat-related CO deaths were in white populations (Ralston and Hampson, 2000).

Type of residence may also play a role in CO poisoning. Liu et al. (2000) investigated risk factors in CO poisoning deaths due to non-automobile sources by conducting an examination of coroners' investigation reports in 270 CO fatality cases. Analyses of the data showed that, compared to individuals living in single family homes, relative risks for fatal CO poisoning were higher among people who lived in multiple unit dwellings, mobile/trailer homes, and temporary shelters. The primary sources were unvented combustion heating appliances and charcoal fuel.

CO Sources in the Home. In the home, major potential sources of CO (as well as other combustion products such as nitrogen and sulfur oxides, VOCs, and particulates) include malfunctioning or inadequately vented or unvented combustion appliances (e.g., such as furnaces, hot water heaters, stoves/ovens, kerosene space heaters, fireplaces and woodstoves, and gas dryers), charcoal or gas grills and other combustion devices that should not be used indoors (e.g., gasoline-powered generators, engines, or tools), and the start-up and idling of vehicles in attached garages (EPA, 2000; Raub et al., 2000; Garrett et al., 1999b). Tobacco smoke can also contribute to CO levels in indoor air, although, unless other sources are present, the increase in CO levels associated with tobacco smoke is typically insufficient to cause CO alarms to sound (EPA, 2000). Because unvented gas cooking ranges/ovens are used intermittently for cooking purposes, it is not likely their use would result in substantial increases in CO over long periods of time, except possibly in households where gas ovens are used improperly as a primary or secondary source of heat (EPA, 2000a). Carbon monoxide in the indoor environment from vented combustion appliances (furnaces, hot water heaters, and gas clothes dryers) is generally negligible unless the unit is malfunctioning (EPA, 2000a). Other residential hazards associated with CO poisoning include: housing design (e.g., lack of proper ventilation in attached garages and conditions which create backdrafting); lack of maintenance and yearly professional inspection of gas, oil, or wood burning appliances and their vent systems; lack of carbon monoxide alarms; and behavior (e.g., warming the car engine in a closed garage, misuse of heating and combustion appliances, cigarette smoking).

Backdrafting. CO levels can become elevated in buildings where backdrafting is occurring. Backdrafting occurs when the air pressure within a home is lower than the air pressure outside, a phenomenon known as house depressurization. When these conditions exist, flue combustion gasses (CO, CO_2, NO_2, etc.) can reverse direction, spilling into the living area of a home instead of traveling up a vent or chimney. Buildings with a relatively tight envelope (few sources for air to enter) and high exhaust capacity are especially prone to depressurization. Appliances with passive ventilation via a draft hood (e.g., water heaters) may also be particularly susceptible to backdrafting. Backdrafting may be triggered by a constricted or poorly functioning chimney, improperly designed or maintained venting systems, or suction created by the operation of household equipment such as exhaust fans, clothes dryers and fireplaces (Nagda et al, 1996; CMHC, 1998). Visual clues like soot on cobwebs and excess moisture can indicate a backdrafting problem. Condensation on windows and other moisture problems result from the water vapor that is produced when burning most fuels. Nagda, et al. (1996) reviewed literature

devoted to this subject and found that, while the causes of house depressurization and backdrafting are well understood, additional research is needed on the frequency, duration, and severity of depressurization-induced spillage events in a broad cross-section of houses.

Lead and Other Inorganic Exposures. As discussed in Section 3.2.4 of this report, lead is an important neurodevelopmental toxicant at relatively low exposure levels in residential settings. At higher levels of lead exposure, more pronounced health effects can also occur, including anemia, kidney injury, nerve injury, brain dysfunction, seizures, coma, and even death (ATSDR, 1999). However, due to lead poisoning prevention legislation and widespread public health interventions, fatal pediatric lead poisoning is now relatively rare in the U.S. (CDC, 2001). Nonetheless, the risk for acute lead poisoning does remain high in some neighborhoods and populations, including children living in older housing with deteriorated leaded paint, in instances involving sanding or stripping of lead-based paint, or where visible deterioration of lead-based painted residential building components is combined with children who exhibit pica tendencies. Acute injuries to children as a result of lead exposure have been recently documented. For example, the CDC recently documented a fatal pediatric lead poisoning case in New Hampshire, in which a two-year old girl died from lead encephalopathy after short-term (less than three weeks) exposure to extremely high levels of lead from dust and deteriorated paint in an older apartment being rented by the family (CDC, 2001). Su et al. (2002) also described three children living in New York City who developed lead poisoning from the ingestion of leaded paint chips. Although the children did not exhibit overt symptoms (fewer than 5% of children with lead poisoning are found to have lead poisoning solely based on their clinical presentation), blood lead levels in excess of 60 μg/dL were found for all during routine medical examinations. Subsequent investigations of each child's place of residence revealed multiple housing violations requiring lead abatement. In one of the cases, the child's permanent residence was lead free and a brief visit to the grandparent's house was the source of the lead paint exposure. Reith et al. (2003) investigated a series of nine patients with clinically significant lead poisoning who required inpatient management (median serum lead levels ere 2.5 micro mol/L (range 1.38-4.83), identified through a Clinical Toxicology Service. Investigations of the cases showed that eight of the children received lead exposures from lead-based paint, with seven of the cases a result of dust exposures from sanded lead paint during house renovations.

3.3.5 Biological Attributes of Housing/Neighborhoods Associated with Injury

Rodents. A potentially fatal respiratory disease, Hantavirus pulmonary syndrome (HPS), is a biological exposure carried by rodents that in some cases may associated with housing and neighborhood conditions. HPS was first identified in 1993 among residents of the southwestern United States, and since, has been responsible for approximately 20–50 cases of HPS annually in the United States (CDC, 2002). Fatality rates for HPS approach one-third, although known Hantavirus infections occur primarily in adults (CDC, 2002). All Hantaviruses known to cause HPS are carried by the New World rats and mice in the Sigmodontinae family, including at least 430 species of mice and rats throughout North and South America (CDC, 2002). Most of the wild rodents in this family are not generally associated with urban environments (versus house mice and the black and Norway rats), although some species (e.g., deer mouse and whitefooted mouse) will enter human habitation in rural and suburban areas (CDC, 2002). As discussed elsewhere in this paper, rodent exposure in homes have been related to numerous factors such as

condition of home (e.g., holes in walls), access to food and water sources in the home, and home sanitation (See section 3.4.3 and 3.4.5).

Mold. As noted previously, Section 3.2.5 of this review (neurodevelopmental effects), other health effects beyond respiratory symptoms have been researched in relation to exposures resulting from damp environments (e.g., molds and bacteria), including nervous system effects, suppression of the immune response, and hemorrhage in the mucous membranes of the intestinal and respiratory tracts (NAS, 2004).

3.3.6 Neighborhood Attributes and Other External Factors Affecting Housing Associated with Injury

Numerous attributes of neighborhoods were linked in the literature to the incidence of pediatric injury. These included conditions of the housing in the neighborhood, location (urban vs. rural vs. suburban), community design and sprawl, traffic and pedestrian/bicycle access, recreational facilities, water features in the area, and socioeconomic characteristics of neighborhoods.

Several studies were identified that attempted to examine the relative importance of individual versus community level risk factors on injury rates (Cubbin et al., 2000; O'Campo et al., 2000; Reading et al., 1999). Some found that neighborhood level characteristics may have an effect on injury independent of individual characteristics. For example, Cubbin et al. (2000) analyzed vital statistics data, census data (including socioeconomic status, racial concentrations, residential stability, urbanization, and family structure), and data from the National Health Interview Survey (NHIS) for 472,364 adults aged 18-64 to examine the relative contributions of individual and neighborhood level risk factors on injury mortality. The authors found that after adjusting for individual variability, community characteristics had an independent effect on the risk of injury. Although this study focused on adults, it suggests that injury is a function of both the characteristics of the individual and of the place in which they live. In contrast, in a population based study of injuries in preschool age children in and around Norwich, UK, Reading et al. (1999) observed that although accidental injury rates were much higher in deprived urban neighborhoods, much of the variability was explained by individual level characteristics.

Neighborhood Location. Residence location has been associated with the risk of various types of injury. For example, the risk of injury from falls may be greater for young, urban children. Stone et al. (2000) investigated the incidence of falls from windows in urban and suburban areas in Hamilton County, Ohio. The study included analysis of hospital records of 1,363 children less 15 years old that went to the hospital for a fall from 1991 through 1997. Results of the analysis indicated that over the 7-year study period, 86 (6.3 percent) of the falls were from windows, and that children 0-4 years old had a higher rate of falls than children aged 5-14. In addition, the prevalence of falls in the urban area was four times that of the surrounding non-urban area, and Black children were three times more likely to fall than non-Black children (Stone et al., 2000).

Youth in rural areas have also been observed to be at risk for injury, particularly those living and working on farms. In a review study, Perry (2003) found that approximately 103 farm fatalities and over 30,0000 nonfatal injuries (e.g., toxic exposures, musculoskeletal trauma, skin disorders,

occupation-induced hearing loss, and stress) occur annually in youth under the age of 20 who live or work on U.S. farms. Data also indicated that although children working in agriculture make up only about 8 percent of the population of working minors in the U.S. overall, they account for up to 40 percent of the work-related fatalities. In an analysis of data from 1994 to 1998, the National Fire Protection Association found that residential fires and fire deaths differ by community size, with rural areas having the highest fire death rates (Ahrens, 2001b). Per capita rates of fire deaths dropped to their lowest in communities with population of 10,000 to 24,999. Rates of fire death were found to increase again in larger cities, but the urban rates still remained far below the rural rates (Ahrens, 2001b).

Other injury risk factors that are a function of neighborhood location, such as traffic, pedestrian/bicycle access, and proximity to water features, are discussed below.

Urban Sprawl, Traffic, and Pedestrian/Bicycle Access. One study was identified in this literature search that specifically examined the relationship between urban sprawl and traffic fatalities. Ewing et al. (2003a) developed a sprawl index and applied it to analysis of traffic and pedestrian fatalities in 488 U.S. counties in the largest 101 metropolitan areas. Urban sprawl had a significant effect on traffic and pedestrian fatalities, with every 1 percent increase in the index (i.e., more compact, less sprawl) associated with a 1.47 to 3.56 percent reduction in pedestrian fatality rates.

Traffic factors were investigated in several studies identified in this literature search (Kraus et al., 1996; Mueller et al., 1990; Tester et al., 2004; Macpherson et al., 1998). For example, to examine to identify traffic and other risk factors for childhood pedestrian and bicyclist injuries, Kraus et al. (1996) conducted a retrospective study of children aged 0-14 years in Long Beach, California. Demographic, clinical, and situational information was extracted from hospital, police, and coroner's records for 228 children who were involved in an auto versus pedestrian or bicyclist incident between 1988 and 1990. Results of the investigations showed that although most incidents happened on residential streets, the risk of injury was greatest on larger boulevards, and tended to cluster by region within the city. Sites where the accidents occurred generally had a larger proportion of traffic exceeding posted speed limits, and were also four times more likely to be near a convenience store, gas station, or fast food store than control sites. Mueller et al. (1990) conducted a similar investigation in King County, Washington of 98 children (aged less than 15 years) that were involved in pedestrian-motor vehicle collisions resulting in death or injuries severe enough to require hospitalization during 1985-86. An analysis was conducted of various environmental and traffic characteristics that were gathered from visits to the neighborhoods of all subjects. Results showed that, although areas with busier streets (greater posted vehicle speeds and/or greater traffic volumes) were generally associated with increased risk for pedestrian injuries, the lack of pedestrian crossing devices, crosswalks, or sidewalks was not associated with an increased risk. To estimate children's exposures to traffic (number of streets crossed) and to investigate the role of these exposures in pediatric pedestrian injury, Macpherson et al. (1998) conducted a study of 4,080 first- and fourth-grade children in 43 Montreal schools. Results (based on analysis of questionnaire-collected information and police reports) suggested that child pedestrian injury rates were positively correlated with the number of streets crossed, and that the number of streets a child had to cross was inversely related to socioeconomic status. Finally, in a matched case-control study over a 5-year period among children seen in a pediatric emergency department after being struck by an automobile, Tester et

al. (2004) attempted to evaluate the effectiveness of speed humps in reducing child pedestrian injuries in residential neighborhoods. Results showed that speed humps were effective at making a child's neighborhood environment safer – they were associated with a reduced risk of children being injured within their neighborhood and being struck by a car in front of their home.

Recreational Facilities. Characteristics of recreational areas have also been investigated in terms of childhood injury rates. In a study of the effectiveness of modern safety surfaces in playgrounds, Norton et al. (2004) found that no serious head injuries occurred in municipal playgrounds over five years of injury surveillance after safety surfaces were installed. Nixon et al. (2003) conducted a study in Brisbane, Australia to investigate the relationships between child injury rates and the frequency of use of playground equipment, including overall and for particular types of equipment. Injury data was collected on children observed at play on five different pieces of playground equipment in a random sample of 16 parks and 16 schools over the course of two years. Results of the study showed that the annual injury rate for the 16 schools and 16 parks under observation was low overall, with 0.59 injuries per 100,000 uses of equipment in schools and 0.26 per 100,000 uses of equipment in parks. The most frequently used types of playground equipment was climbing equipment (3,762 uses), followed by horizontal ladders (2,309 uses), and slides (856 uses). The authors suggest that the annual number of injuries per standardized number of uses could be used to determine the relative risk of particular pieces of playground equipment. Petridou et al. (2002) conducted a case-control study to identify and quantify specific risk factors for injuries in playgrounds. Through analysis of data from an Emergency Departments Injury Surveillance System (EDISS) of hospitals in Greater Athens, Greece during 1999, the authors identified 777 injuries in public and private playgrounds out of a total of 17,497 injuries reported in the system. In a sample of 294 of the children, patterns of type of playground use were assessed. Results of the analysis showed that the annual incidence of playground injuries was about 7 in 1000 among boys and 4 in 1000 among girls, with a 2.2 times higher risk for an injury in public than in private playgrounds. The authors suggest that public playgrounds in Greater Athens differ from private ones, because the former generally have more equipment, usually of greater height, with less resilient surfaces, and supervision relies mainly on parents or guardians. The study also showed that children in public playgrounds had an eight times higher odds for concussion and six times higher for open wounds relative to children at private playgrounds. The types of equipment most frequently associated with injuries were swings, slides and seesaws.

Water Features. Browne et al. (2003) examined risk factors involved in 883 non-bathtub drownings among New York state residents from 1988 to 1994 using medical examiner, coroner, police, and/or hospital records. Although the majority of drownings occurred in a natural body of water for all age groups, most drownings among children ages 0-4 years occurred in residential swimming pools, with the child typically gaining access to the pool via inadequate fencing, an open or ineffective gate, or a ladder (to an above-ground pool) left in the down position. As previously discussed in Section 3.3.3, Brenner et al. (2003) also found similar evidence in a literature review that lack of swimming safety devices (e.g., pool fences, pool alarms) was a major risk factor in child pool injuries.

3.3.7 Behavioral and Socioeconomic Mediators Associated with Housing/Neighborhoods and Injury

Socioeconomic status (SES) was frequently investigated in the literature in relation to risk factors for injury in children. Numerous studies found SES to be a strong predictor of injury. For example, Durkin et al. (1994) studied the relationship between socioeconomic disadvantage and the incidence of severe childhood injury during a nine year period (1983 through 1991) in Northern Manhattan, New York. Analyses of census tract data indicated that SES factors such as proportion of low-income households, single-parent families, non-high school graduates, and unemployment were all significant predictors of risk for both unintentional and intentional injury. However, the single most important predictor of all injuries was low income. For example, children living in areas with predominantly low-income households were more than twice as likely as those living in predominantly higher-income areas to be injured. As noted previously, Cubbin et al. (2000) also found that community characteristics, including SES, had an independent effect on the risk of injury in an analysis of vital statistics data, census data (including socioeconomic status, racial concentrations, residential stability, urbanization, and family structure), and data from the National Health Interview Survey (NHIS). In a review study, Cubbin and Smith (2002) examined the body of literature on SES as a determinant of injury and observed that although a higher SES has a strong inverse association with the risk of fatal injuries, the relationship between SES and nonfatal injuries is less consistent.

Several studies identified in this literature search also suggested that non-income characteristics associated with low SES may play a role in childhood injury. For example, O'Campo et al. (2000) looked at injury rates in relation to neighborhood economic and physical characteristics in three low-income communities in Baltimore, Maryland. Data were collected on select neighborhood characteristics (average per capita income, rate of housing violations, and crime rate), and via a survey administered to 288 households to gather injury event information. Results showed that although all three communities were low-income, variations in neighborhood characteristics influenced injury prevalence rates. Most significantly, higher rates of housing violations in the neighborhood were associated with an increased risk of injury in children under five years old in the household. In a similar study (although of broader scope with regard to health outcomes), Cohen et al. (2003) found that although SES status is associated with mortality, it does not fully explain health disparities. Using data from the Project on Human Development in Chicago Neighborhoods (PHDCN), an examination was conducted for 8,782 residents in 343 Chicago neighborhoods of neighborhood-level factors associated with premature mortality, including concentrated disadvantage, residential stability, immigrant concentration, "collective efficacy" (a measure of willingness to help out for the common good), and "broken windows" (boarded up stores and homes, litter, and graffiti). Both collective efficacy and broken windows appeared to mediate the effect of concentrated disadvantage on all-cause premature mortality. In a population based study of injuries in preschool age children in and around Norwich, UK, Reading et al. (1999) observed that although accidental injury rates were much higher in deprived urban neighborhoods, much of the variability was explained by individual level characteristics. Similarly, Shenassa et al. (2004) conducted an investigation of specific factors beyond SES that may influence the increased childhood injury rates that are observed in disadvantaged neighborhoods. Result of the study indicated that individual level housing characteristics partially mediate the associations between community characteristics (e.g., concentration of poverty) and childhood injury. In addition, hierarchical models suggested that

housing characteristics are significant predictors of pediatric injury, independent of other community level SES risks.

3.3.8 References for Section 3.3

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3.4 LITERATURE ON THE RELATIONSHIPS BETWEEN HOUSING AND NEIGHBORHOOD CHARACTERISTICS AND ASTHMA

3.4.1 Additional Information on the Literature Review Approach for Asthma

Hypothesis 4 of the National Children's Study addresses asthma (see Appendix A). Specifically, Hypotheses 4.1, 4.2, 4.3, and 4.5 address asthma risk factors that potentially relate to the focus of this paper – housing and neighborhood characteristics. These housing/neighborhood related risk factors for asthma include indoor and outdoor air pollution and bioaerosols (Hypothesis 4.1), viral infection (Hypothesis 4.2), maternal stress during pregnancy (Hypothesis 4.3), and the hygiene hypothesis (Hypothesis 4.5).

The primary outcome of interest described in Hypothesis 4 is asthma, although for the purposes of this literature review both asthma and other adverse respiratory outcomes were examined in the literature. Furthermore, although Hypothesis 4 as currently drafted focuses primarily on a limited set of chemical and biological risk factors, this literature review was conducted with a broader scope and allowed for the inclusion of other housing and neighborhood risk factors that were reported in the literature to be associated with asthma or exposures of concern for asthma, such as housing type (e.g., multiple unit dwellings), housing conditions, type of heating system in the dwelling, etc.

3.4.2 Overview

More than 20 million people in the United States, including 9 million children less than 18 years of age, are estimated to have asthma (Dey et al., 2004). Among children, it is the most common chronic illness (NAS, 2000). A substantial body of research, including population-based studies of school-aged children and young adults, indicates that the prevalence and severity of asthma have increased dramatically over the last several decades in the United States and many other parts of the world (CDC, 1998; Carter and Platts-Mills, 1998; Platts-Mills, 1998). These increases in asthma prevalence and severity have occurred despite general reductions in levels of most air pollutants outside; therefore, many researchers hypothesize that coinciding changes in the home environment are potentially influential, and possibly more important, factors in determining asthma risk (Custovic et al., 1998).

Structural or physical housing characteristics have been associated with increased exposure to both biological and chemical variables implicated in the causation and exacerbation of asthma. In particular, newer tighter housing designs intended to increase energy efficiency, the presence of extensive furnishings and carpeting, and moisture problems have all been cited as conditions in the home that have the potential to affect indoor air quality and the prevalence and severity of

asthma (NAS, 2004; Platts-Mills et al., 1997; Platts-Mills, 1998; Carter and Platts-Mills, 1998; Custovic et al., 1998).

While the potential impacts of indoor air quality on respiratory health have been studied extensively, some researchers are taking an even broader approach to the investigation of asthma and other respiratory triggers by focusing on behavioral, socioeconomic, and neighborhood characteristics. Residence in an inner-city environment, for example, has been closely associated with the structural characteristics and other housing-related variables thought to increase asthma risk (Brugge et al., 2003; Krieger et al., 2000).

An overview of the research identified in the course of this literature search on housing and neighborhood characteristics associated with asthma and other adverse respiratory health outcomes is presented in Table 3.4-1 below

Table 3.4-1. Summary of Key Literature on Housing and Neighborhood Characteristics Associated with Asthma and Respiratory Health

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
GENERAL STUDIES AND REVIEWS		
General Housing	Increases in asthma prevalence and severity have occurred despite general reductions in levels of most air pollutants outside; coinciding changes in the home environment may be important factors	Custovic et al. 1998
	Structural and physical housing characteristics have been associated with increased exposure to both biological and chemical variables implicated in the exacerbation and causation of asthma	NAS 2004; Platts-Mills et al. 1997; Platts-Mills 1998; Carter and Platts-Mills 1998; Custovic et al. 1998
General Neighborhood		
HYPOTHESIZED STRUCTURAL/PHYSICAL RISK FACTORS		
Housing type, crowding, and age	Residing in densely populated areas increased the likelihood of elevated cockroach allergen levels in the home	Leaderer et al. 2002
	Cockroach allergens were more likely to be at higher levels in multi-family homes, especially in high-poverty regions of large metropolitan areas	Kitch et al. 2000; Arruda et al. 2001
	Mouse allergen concentrations were associated with building type, with higher levels detected in apartment buildings having fewer than eight floors	Chew et al. 2003
	The National Survey of Lead and Allergens in Housing found high concentrations of mouse allergen to be most common in mobile homes, high-rise apartments, duplex or triplex buildings, and homes built prior to 1945	Cohn et al. 2004
	Dust mite allergen concentrations were 1.9-2.4 times higher in the autumn than in the spring; levels in beds in single-dwelling houses were 19-31 times higher than in apartments, far outweighing observed seasonal effects	Chew et al. 1999
	Crowding was associated with a 60% reduction in the incidence of asthma and a 2 1/2-fold increase in the incidence of lower respiratory tract infections in Sao Paulo	Cardoso et al. 2004
	Home dampness problems increased with building age and deterioration, although some modern construction techniques and materials also can increase the risk of dampness problems	NAS 2004
	Relatively new apartment buildings and single-family homes with crawl space/concrete slab foundations were associated with recurrent wheezing in infants	Emenius et al. 2004

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
Structure, construction, condition	High levels of mouse allergen in inner-city apartments were associated with the presence of holes in walls or ceilings	Chew et al. 1999
	Elevated levels of cockroach allergens in inner-city housing were associated with the degree of dwelling disrepair	Chew et al. 2003; Rauh et al. 2002
	Pest allergens were found to be a potentially important factor in asthma exacerbation in any area where deteriorated or substandard housing permits infestation, including rural areas, suburbs, and small towns and cities across the United States	Arruda et al. 2001
Electrical system		
Fire Related Factors		
Building Materials	The risk of bronchial obstruction was related to the presence of polyvinyl chloride (PVC) flooring and textile wall materials	Jaakkola et al. 1999
	Emissions from plastic wall materials indoors may have adverse effects on the lower respiratory tracts (but not upper respiratory) of small children, and may increase risks of asthma and pneumonia	Jaakkola et al. 2000
	New linoleum flooring, synthetic carpeting, particleboard, wall coverings, furniture type, and recent painting were related to increased risks of asthma, wheezing, and allergy	Jaakkola et al. 2004
HVAC	The presence of air-conditioning increased the risk of dampness problems	NAS 2004
	Air conditioning and dehumidifiers reduced dust mite and allergen concentrations in homes in a temperate climate during the summer season	Arlian et al. 2001
	The absence of air conditioning was associated with increased dust mite allergen concentrations	van Strein et al. 2004
	The use of forced air heating systems was inversely related to dust mite allergen and airborne fungi concentrations in several studies	Li and Kendrick 1995; Arbes et al. 2003; Peterson et al. 2003
	Reported allergic symptoms were less severe in residents of homes with forced air heating systems, air filters, air conditioners, and humidifiers installed within the furnace	Li and Kendrick 1995
	Installation of central heating systems and insulated windows was associated with increased dust mite allergen and mold spore concentrations	Hirsch et al. 2000
	Low ventilation rates in homes strengthened the effects of indoor air pollutants (e.g., environmental tobacco smoke) in increasing bronchial obstruction risks	Oie et al. 1999
	Air exchange rate and type of ventilation system in the home did not directly affect the risk of recurrent wheezing in infants	Emenius et al. 2004
Moisture	Indoor dampness/water damage was associated with numerous respiratory health effects, including asthma, allergic symptoms, wheeze, cough, and other respiratory symptoms	Garrett et al. 1998; Kilpelainen et al. 2001; Li and Kendrick 1995; Spengler et al. 2004
	The risk of current asthma, allergic rhinitis, and atopic dermatitis was found to be higher in damp homes with visible mold, damp stains, or water damage	Kilpelainen et al. 2001
	Review: Much evidence exists to link indoor dampness with respiratory health effects, though the relative effects of dampness or particular dampness-related agents are not yet well understood	Bornehag et al. 2004; NAS 2004
	Features of houses associated with increased moisture levels include: lack of central heating, low temperatures, below-grade spaces or being on the ground floor level, poor ventilation, excess production of water in the house (e.g., humidifiers, unvented cooking), presence of pets, and water leakage or flooding	NAS 2004
	Elevated indoor humidity and reported wintertime windowpane condensation were associated with recurrent wheezing in infants	Emenius et al. 2004
	Moisture level is among the most important factors affecting mold growth in homes; most molds require fairly wet conditions (near saturation), lasting for many days, to extensively colonize an environment	NAS 2000
	Increased levels of airborne fungi were consistently observed when residential water problems lasted beyond three days	Li and Kendrick 1995
	Musty odor, water intrusion, high indoor humidity, and limited ventilation through open windows were associated with large airborne fungal spore concentrations	Garrett et al. 1998
	Indoor relative humidity is positively associated with dust mite allergen levels	Peterson et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Humidity is a limiting factor in dust mite growth	NAS 2000
	See "HVAC" row above	NAS 2004
	Home humidity is an important factor in cockroach infestations for some species; German and American cockroaches tend to aggregate in warm, humid crevices (e.g., around water heaters, laundries, bathrooms, and appliances); Oriental cockroaches prefer damp areas (e.g., basements, plumbing fixtures, and sewers	Eggleston and Arruda 2001
	Concentrations of cockroach allergen are typically highest in kitchens and bathrooms (i.e., where food and water sources are plentiful)	NAS 2000; Eggleston and Arruda 2001
	Releases from formaldehyde-containing materials and furnishings can increase with the humidity and temperature of the surrounding air, and age of product	Godish and Rouch 1986; NAS 2004; Wiglusz et al. 1990; Wiglusz et al. 1991; Wiglusz et al. 1995
Cleanliness	Lack of sufficient cleaning, excess clutter, and failure to properly store food items can attract cockroaches, a common allergen in inner-city environments	Kattan et al. 1997
	Dust may serve as a reservoir for endotoxins	Gehring et al. 2004
	Endotoxin levels were positively associated with steam cleaning or shampooing the carpet, presumably due to increases in relative humidity of the carpet	Wickens et al. 2003
	Vacuuming plus dry steam cleaning and vacuuming alone resulted in significant reductions in dust mite allergen concentrations and loads in carpets; however, increased moisture levels with steam cleaning may also exacerbate dust mite and mold growth	Vojta et al. 2001
Home Furnishings	Increased fungal levels were associated with carpets	Li and Kendrick 1995
	Upholstered furniture, carpeting, mattresses, and pillows may be one of the primary determinants of dust mite growth in homes	Vaughan and Platts-Mills 2000
	Carpet underlay less than 8 mm thick was associated with an almost 3-fold increase in dust mite allergen levels when compared with thicker carpet underlays	Wickens et al. 2001
	Home floor characteristics (smooth versus carpeted floors) were significant predictors of allergen levels	Chew et al. 1998
	Home furnishings such as carpets or textile wall coverings can contribute to degraded indoor air quality through off-gassing of chemicals (e.g., formaldehyde)	Jaakkola et al. 2004
	New carpets and upholstered furniture have been found to be a potential source of formaldehyde, which has been linked to respiratory symptoms	Garrett et al. 1999; Godish and Rouch 1987
Safety devices		
HYPOTHESIZED CHEMICAL RISK FACTORS		
Pesticides	Pesticide exposure has been associated with asthma/airway constriction in adults in occupational settings	Etzel 1995; CDC 2003
	Pyrethroid pesticides applied via ground spraying to neighborhoods for West Nile virus/mosquito control were linked to asthma in case reports from New York in 2000	CDC 2003
	Pesticide spraying in New York in 2000 was not associated with population-level increases in public hospital emergency room visit rates for asthma	Karpati et al. 2004
	Pesticides may be related to the occurrence of asthma in children because they disrupt the part of the nervous system that regulates functioning of the lungs	Eskenazi et al. 1999
	Pesticides used to fight insect and rodent infestations (for allergen/asthma control) have sometimes created toxic exposure hazards	Bashir 2002
	Children in agricultural areas are potentially exposed to higher pesticide levels than other children (e.g., because of pesticides tracked into their homes by household members, pesticide drift, or by playing in nearby fields)	Eskenazi et al. 1999
	Pesticides have been found to be of particular concern in low-income, inner-city areas, where conditions favor pest infestation and, consequently, pesticide usage	Berkowitz et al. 2003
Other organic chemicals	Review (through 1999): No indoor chemical exposures are conclusively linked with asthma development; limited evidence exists linking formaldehyde and fragrance exposures and asthma exacerbation	NAS 2000

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	The risk of bronchial obstruction was related to the presence of polyvinyl chloride (PVC) flooring and textile wall materials	Jaakkola et al. 1999
	Elevated indoor formaldehyde and VOC concentrations were associated with asthmatic symptoms and airway inflammation/wheezing	Norback et al. 1995; Wieslander et al. 1997; Venn et al. 2003
	Common indoor sources of formaldehyde included particle board (e.g., applied as subflooring), plywood, wood paneling, urea foam insulation, and some carpets, furniture, and upholstery fabrics.	Garrett et al. 1999; Godish and Rouch 1987; Wiglusz et al. 1991
	Certain types of paint can be sources of formaldehyde and VOC emissions	Wieslander et al. 1997
	Risks of current asthma, wheezing, and allergy were related to recent renovation and the installation of materials with potential chemical emissions, including new linoleum flooring, synthetic carpeting, particleboard, wall coverings, and recent painting.	Jaakkola et al. 2004
	Also see "Moisture" row above	Godish and Rouch 1986; etc.
Combustion by-products	Review: Combustion by-products were linked to asthma-related symptoms, especially short-term high-level exposure to nitrogen dioxide	NAS 2000
	Infants living in homes with nitrogen dioxide concentrations exceeding 17.4 ppb had a higher frequency of days with wheeze, persistent cough, and shortness of breath	Van Strein et al. 2004
	Nitrogen dioxide exposure was positively related to the intensity of virus-induced asthma exacerbation in children	Chauhan et al. 2003
	Indoor levels of nitrogen dioxin were higher than outdoor levels, and varied with season (with the highest levels in the winter); major indoor sources observed were: gas stoves, vented gas heaters, and smoking	Garrett et al. 1999
	The use of a gas oven or stove for heat was associated with doctor-diagnosed asthma	Lanphear et al. 2001a
	Gas stove use was a significant risk factor for respiratory symptoms independent of nitrogen dioxide levels, suggesting that gas stoves may present other risks apart from nitrogen dioxide emissions	Garrett et al. 1998
	Household gas cooking was positively associated with respiratory illnesses	Wong et al. 2004
	Family indoor and outdoor environment (e.g., farm location) were confounding factors in determining the association between respiratory symptoms and combustion appliances	Kilpelainen et al. 2001
	Carbon monoxide has been correlated with asthma exacerbation in several studies, but the relationship between short-term low levels of carbon monoxide and respiratory disease cannot yet be interpreted with confidence	EPA 2000
	CO may be a marker for other combustion products which exacerbate asthma	EPA 2000; Sheppard et al. 1999; Norris et al. 1999
Lead		
Asbestos, fiberglass		
Other inorganic chemicals		
Also see "Ambient air pollution" and "Traffic" rows under External Factors Affecting Housing		
HYPOTHESIZED BIOLOGICAL RISK FACTORS		
Multiple allergens	Pest allergens were an important factor in asthma exacerbation in areas where deteriorated/substandard housing permitted infestations	Arruda et al. 2001
	Mouse allergens were positively associated with cockroach infestations because both types of pests have similar environmental requirements (e.g., means of access to the home, food, and water)	Phipatanakul et al. 2000a
	Epidemiologic studies demonstrate a strong association between exposure to indoor allergens and allergic sensitization	Arshad 2003; Finn et al. 2000; Gold 2000
	Sensitization occurs at different exposure levels for various allergens	Murray et al. 2001

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Slightly elevated levels of multiple allergens may have an even greater effect on respiratory symptoms than exposure to very high levels of just one allergen	Gehring et al. 2001
	Nearly 45% of doctor-diagnosed asthma can be attributed to residential risk factors such as dust mite, cockroach, and pet allergens	Lanphear et al. 2001b
Dust mites	Review: There is sufficient evidence that a causal relationship exists between house dust mite exposure and the development of asthma in susceptible children	IOM 1999
	Evidence supporting an association between exposure to dust mite allergens and asthma exacerbation is well documented in the general literature	NAS 2000; Custovic et al. 1998; Platts-Mills et al. 1997
	Review: 50-60% of middle-class or mixed economic-class asthmatic children had positive skin test results to dust mites	Kattan et al. 1997
	National Survey of Lead and Allergens in Housing: >80% of U.S. homes have detectable levels of house dust mite allergen and allergen levels associated with allergic sensitization and asthma exacerbation are common	Arbes et al. 2003
	Children with a family history of allergic sensitization are susceptible to even very low levels of exposure to dust mites and other indoor allergens	Wahn et al. 1997
	Most dust mite exposure is thought to occur via larger (~10-25 μm) dust particles that become airborne during and immediately after disturbance of dust reservoirs	NAS 2000
	The primary determinants of dust mite growth in homes are food source (i.e., skin scales), temperature, humidity and the availability of upholstered furniture, carpeting, mattresses, and pillows	Vaughan and Platts-Mills 2000
	See "Moisture" row above	NAS 2000; Peterson et al. 2003
	Mites are a very common allergen exposure source in temperate and humid regions such as the southeastern United States	Curtis et al. 1997
	The critical humidity level for mite survival is temperature dependent and ranges from 55% to 73% humidity for temperatures between 15°C and 35°C	Arlian et al. 2001
	Features of houses that can increase mite growth include: poor ventilation, excess production of water in the house (e.g., humidifiers, unvented cooking), water leakage, poor cleaning habits, and being on the ground floor level	NAS 2000
	Family size has been positively associated with mite allergen levels	Peterson et al. 2003; Wickens et al. 2001
	The presence of floor insulation was associated with lower dust mite allergen levels	Wickens et al. 2001
	Exposures during infancy to dust mite allergen concentrations above 2 μg/g and 10 μg/g of house dust were associated with sensitization and exacerbation, respectively	Sporik et al. 1990
	House dust mite sensitization and asthma were related, but no relationship between dust mite allergen exposure in early childhood and asthma development was found	Carter et al. 2003
	Residing in densely populated areas increased the likelihood of elevated cockroach allergen levels in the home	Leaderer et al. 2002
	Cockroach allergens were found at higher levels in multi-family homes, often in high-poverty regions of large metropolitan areas	Kitch et al. 2000; Arruda et al. 2001
Cockroaches	Level of cockroach allergens within housing units in the inner- city was strongly associated with the degree of dwelling disrepair	Chew et al. 2003; Rauh et al. 2002
	Home humidity was an important factor in cockroach infestations for some species	Eggleston and Arruda 2001
	Over 50 cockroach species occur in the U.S., with five species common in residential settings	Eggleston and Arruda 2001
	Cockroach allergens are associated with larger dust particles that are only airborne during and immediately after disturbances of dust reservoirs; concentrations are typically highest in kitchens and bathrooms, and sometimes bedrooms	NAS 2000; Eggleston and Arruda 2001
	Cockroach allergens are an important source of allergic sensitization, particularly in areas where cockroach infestation is common	NAS 2000; Chapman et al. 1997
	Sensitization to cockroach allergens may develop earlier in childhood and be more prevalent than previously realized	Alp et al. 2001
	Exposure to cockroach allergens at three months of age is tied to measurable allergic response by the age of two years	Finn et al. 2000

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Exposure to cockroach allergen early in life may contribute to the development of asthma in susceptible children	Litonjua et al. 2001
	Over 40% of a middle-class, suburban study population had elevated levels of cockroach allergens in their homes	Matsui et al. 2003
	Cockroaches thrive in temperate/humid regions, but also succeed in northern states	Chapman et al. 1997
	Cockroach allergens were at higher levels in multi-family homes, often in high-poverty regions of large metropolitan areas	Kitch et al. 2000; Arruda et al. 2001
	In the National Cooperative Inner City Asthma study (NCICAS), cockroach allergen was the second most common sensitizer (36%) in asthmatic children tested	Kattan et al. 1997
	In other studies, positive skin tests to cockroach were uncommon middle-class or mixed economic-class asthmatic children; sensitivity to dust mites and cat or dog dominated in this population	Kattan et al. 1997
	Low socioeconomic status, African-American or Hispanic ethnicity, low maternal education, and residence in densely populated areas were associated with elevated cockroach allergen levels in the home	Leaderer et al. 2002
	See "Structure, construction, condition" row above	Arruda et al. 2001; Rauh et al. 2002
Other insects (ticks, fleas, mosquitoes)		
Mice	Mouse allergens were widely distributed in inner-city homes, with 95% of all homes assessed having detectable mouse allergen in at least one room	Phipatanakul 2000a
	Exposure to mouse allergen was associated with asthma sensitization, particularly in certain inner-city, multiple-family dwellings	Phipatanakul 2000b
	Mouse allergen was common in low income, inner-city apartments, even where sightings were not reported	Chew et al. 2003
	A strong association was documented between the presence of rats or mice in the home and asthma, particularly among Puerto Rican residents	Findley et al. 2003
	National Survey of Lead and Allergens in Housing: Detectable levels of mouse allergen were found in 82% of U.S. homes	Cohn et al. 2004
	Detectable levels of rat allergen were present in 33% of inner-city homes found; there were significantly higher rates of asthma morbidity in children sensitized to rats	Perry et al. 2003
	See "Housing type, crowding, and age" row above	Cohn et al. 2004; Chew et al. 2003
	See "Structure, construction, condition" row above	Chew et al. 1999
Rats Other rodents	IOM 1999 Review: Evidence of an association between exposure to rodents and asthma exacerbation exist from occupational exposure in a laboratory setting only.	NAS 2000
Molds	There are over 200 species of fungi to which people are routinely exposed	NAS 2000
	Mold plays a role in the exacerbation of asthma symptoms, but the association between mold exposure and asthma development remains undetermined	NAS 2000
	Most of the molds do not typically produce toxins (mycotoxins), but they may be important as sources of mold allergens	Etzel 2000
	National Cooperative Inner City Asthma Study: The most common positive mold allergen sensitivity was to Alternaria (38%)	Eggleston et al. 1999; Kattan et al. 1997
	Under the appropriate indoor environmental and competitive conditions (very damp conditions and with appropriate nutrient sources) some molds may be induced to produce mycotoxins; toxin producing molds (e.g., *Stachybotrys chartarum*) may be prominent	Flannigan 1997; Boutin-Forzano et al. 2004; Burge and Amman 1999; NAS 2004
	Self-reported mold was associated with respiratory health using both subjective and objective markers of lung function	Andriessen et al. 1998
	The clearest association between mold exposure and asthma is sensitization to Alternaria (generally regarded as an outdoor mold)	NAS 2000
	Levels of mold in the home were positively associated with wheeze/persistent cough in the first year of life among children whose mothers had asthma	Belanger et al. 2003
	Exposure to high levels of *Penicillium* was associated with higher rates of wheeze and persistent cough in infants.	Gent et al. 2002

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Exposure to high levels of fungal spores was associated with both wheezing and non-wheezing respiratory ailments in infants	Stark et al. 2003
	The presence of mold in homes was associated with numerous respiratory ailments, including bronchitis, asthma, dry cough, and wheezing	Spengler et al. 2004
	Relationships between exposure to mold and respiratory symptoms of children are complicated and may depend on a variety of potentially confounding factors, such as the season in which mold samples were obtained	Gent et al. 2002
	Some human case-studies show an association between inhaled mycotoxins and health effects, but these were mostly occupational studies	Burge and Ammann 1999
	Toxins from *Stachybotrys chartarum* were associated with lung inflammation and hemorrhage in animal studies and non-specific symptoms (headaches, sore throats, flu symptoms, diarrhea, fatigue, and dermatitis) in case studies	Nikulin et al. 1996 1997 as cited in Burge and Ammann 1999; Dill et al. 1997 and Croft et al. 1986 both as cited in Burge and Ammann 1999
	Review of in vitro and in vivo research on *Stachybotrys chartarum*: Effects in humans may be biologically plausible, but more research is required	NAS 2004
	Stachybotrys chartarum in indoor environments has been associated with pulmonary hemorrhage deaths in infants	Etzel et al. 1998; Flappan et al. 1999; Elidemir et al. 1999; Vesper et al. 2000
	The association between pulmonary hemorrhage deaths in infants and the presence of *Stachybotrys chartarum* has not been conclusively proven	CDC 2000
	Recent research supports the potential for mycotoxin exposure in the indoor environment to result in adverse effects on respiratory health	NAS 2000; Sorenson 1999 Rao et al. 1996; American Academy of Pediatrics 1998
	Very young children may be especially vulnerable to certain mycotoxins; Exposure to the trichothecene mycotoxins may result in pulmonary capillary fragility in the rapidly growing lungs of children younger than one year	American Academy of Pediatrics 1998; Etzel 2000
	Reviews: Evidence is not sufficient to support the conclusion that inhaled mycotoxins in the home, school, or office environment have an adverse effect on human respiratory health	Hardin et al. 2003; Fung and Hughson 2003
	Modeling maximum feasible inhaled mycotoxin exposures, toxic human health effects following inhalation exposure to mycotoxins in mold-contaminated home, school, or office environments is implausible	Kelman et al. 2004
	The primary factor affecting fungal growth in homes is moisture level; *See "Moisture" row above*	NAS 2000; NAS 2004; Li and Kendrick 1995
	Molds can obtain nutrients and moisture sufficient for growth from water-affected building materials such as wood, insulation materials, cellulose in the paper backing on drywall, glues used to bond carpet to its backing, furniture, clothing, dust and dirt.	Burge and Otten 1999; American Academy of Pediatrics 1998; Bush and Portnoy 2001; Gravesen 1999
	Humidity levels within walls were higher in areas where *Stachybotrys chartarum* was identified compared to areas where other or no molds were identified	Boutin-Forzano et al. 2004
	Fungal levels were highest in living rooms, followed by family rooms, kitchens, bathrooms, and bedrooms; levels increased where carpets were present and decreased where forced-air heating systems, dehumidifiers, air filters, and air conditioners were present	Li and Kendrick 1995
	Surrogate measures of fungal presence in the home were not significantly and consistently related to the presence of fungal propagules measured in indoor air	Ren et al. 2001

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Mold exposure in homes primarily occurs as airborne spores and hyphal fragments, but molds are also present in household dust and on surfaces	NAS 2000
Pets	Review: Sufficient evidence exists to support a relationship between cat and dog allergen and asthma exacerbation, but not for asthma development; studies of pet exposure in early life and asthma development have had conflicting results	NAS 2000
	In some settings (e.g., where cockroach and dust mite allergen exposure is rare), pet allergens are the dominant indoor allergens	Chapman and Wood 2001
	Cat and dog allergens are carried on small (<10 μm) airborne particulates and may remain suspended in the air for long periods of time	Chapman and Wood 2001; NAS 2000
	Cat and dog dander is adherent in nature and is easily transported from room to room in a dwelling	Chapman and Wood 2001; NAS 2000
	Clothing can be a major source/reservoir of inhaled cat and dog allergens	O'Meara and Tovey 2000
	The vast majority of homes contain cat and dog allergen even if a pet has never lived there (due to small particle size and ease of transport)	Arbes et al. 2004
	Pet allergen levels are typically highest in homes housing these animals; occupant choice plays the primary role in determining indoor exposure to pet allergens	Chapman and Wood 2001; Peterson et al. 2003
	Pet allergens were linked to asthma exacerbation and respiratory symptoms, but the exact association is not easy to characterize	Gehring et al. 2001
	Moderate exposure to cat allergen is associated with sensitization, but the overall risk of sensitization appears to decrease with exposure to higher levels of cat allergen	Platts-Mills et al. 2001; Sporik et al. 1999
	Exposure to both dog and cat allergen (at any concentration) in early life was associated with a decreased risk of wheezing in children	Litonjua et al. 2002
	The hypothesized protective effect of high-level cat allergen exposure has not been proven, and appears to diminish when combined with certain genetic factors	Celedon et al. 2002
Bacteria, endotoxins, microbial VOCs	Bacterial growth may occur in water damaged materials and damp areas of homes	NAS 2004
	Bacterial endotoxin exposure at high-levels has been associated with lung disease among workers, but the literature on low-level endotoxin exposures reports both adverse and beneficial effects	NAS 2004
	Endotoxin in house dust was related to the severity of asthma symptoms	Michel et al. 1996
	Farm children who were routinely exposed to high endotoxin levels has a decreased risk of hay fever, sensitization, atopic wheeze, and atopic asthma.	Braun-Fahrlander 2003
	Exposure to endotoxin in house dust was negatively associated with allergic sensitization in children; this protective effect grew stronger with higher endotoxin levels	Gehring et al. 2002
	Exposure to endotoxin increased the risk of wheezing in early life, but the risk diminished with age, and possibly protected against wheezing later in childhood	Litonjua et al. 2002
	Review: The protective effect of endotoxins in asthma has not been proven and endotoxins may only be an indicator for some other environmental variable	Eder and von Mutius 2004
	Airborne endotoxin levels indoors were most strongly affected by presence of dogs, moisture sources (lack of dehumidifier), and increased amounts of settled dust	Park et al. 2001
	Home endotoxin levels were positively associated with dogs inside, number of household occupants, reusing vacuum dust collection bags, steam cleaning or shampooing the carpet, and high relative humidity	Wickens et al. 2003
	Home endotoxin levels were lower with the use of central air conditioning but were not affected by home dampness or cleaning frequency	Gereda et al. 2001
	Mattress dust endotoxin levels were highly variable between homes, but associated with pet-ownership, contact with pets, and number of persons living in the home	Gehring et al. 2004
	There was a dose-dependent association between a child 's activity on the farm and home endotoxin levels	Waser et al. 2004
Other triggers (e.g., viral infections, parasites)	Evidence exists for an association between certain types of viruses and asthma development and exacerbation	NAS 2000
	Viruses are a major trigger for acute asthma attacks in children	Gern 2004
	The relationship between viral infections and asthma exacerbation was affected by exposure to high levels of nitrogen dioxide prior to the infection	Chauhan et al. 2003

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
	Repeated viral infections (non-lower respiratory tract) early in life may reduce the risk of developing asthma up to school age; repeated lower respiratory tract infections in the first three years of life showed a positive association with wheeze up to the age of seven years	Illi et al. 2001
	Flu and fever episodes during pregnancy (mainly the third trimester) were significantly associated with asthma in children	Calvani et al. 2004
	The hygiene hypothesis suggests that children's immune systems are not being developed normally at a young age due to a lack of exposure to infectious agents	Ball 2000; Arruda et al. 2001
	An inverse relationship between atopy-related illnesses and microbial exposure has been observed in several studies	Liu and Szefler 2003; von Mutius 2002; Braun-Fahrlander et al. 2002
	A protective effect of day care attendance was only observed in children without maternal history of asthma	Celedon et al. 2003
	International Study of Asthma and Allergies in Childhood: Contrary to the hygiene hypothesis, asthma prevalence in some underdeveloped countries (i.e., countries with high infection rates) is not lower that those in the developing world	ISAAC Steering Committee 1998; Arruda et al. 2001
	Review: The relationship between the number of siblings in a family and allergic disorders was not consistently explained by the hygiene hypothesis	Karmaus and Botezan 2002
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS		
Location	Residence in the inner-city has been associated with the structural characteristics and other housing-related variables thought to increase asthma risk	Brugge et al. 2003; Krieger et al. 2000
	Differences have been observed in the types of asthma triggers found in homes in inner-city areas compared to suburban or rural areas	Kitch 2000; Kattan et al. 1997
	Inner-city children were more likely to be sensitized to multiple indoor allergens and to live in surroundings associated with allergen exposure	Crain et al. 2002
	Indoor concentrations of many airborne pollutants were higher in urban residences than in suburban homes	Simons et al. 2004
	Elevated levels of pet allergens observed in many homes without pets (particularly among highly pet-owning demographic groups) may be a result of the community serving as an important local source of these pet allergens	Arbes et al. 2004
	Asthmatics living in low income, urban housing have specific sensitivities that differ from other populations, with a higher frequency of sensitivity to cockroaches, mice, and molds and less frequent sensitivity to cats, dogs, and dust mites	Eggleston 2000; Eggleston et al. 1999; Phipatanakul 2000a and 2000b
	Cockroaches may be the sole sensitizing agent for many children living in inner-city areas	Alp 2001
	Living on a farm was found to have a protective effect against allergic rhinitis, and also (but more weakly) against asthma and wheezing irrespective of family size	Kilpelainen et al. 2000
Zoning/building codes		
Ambient air pollution	Asthma and bronchial hyper-responsiveness were significantly associated with living in a polluted industrialized environment, though atopy was not	Kim et al. 2001
Traffic	Clusters of asthma cases were observed surrounding high-traffic areas and suspected emissions sources	Oyana and Lewbuga-Mukasa 2004
	Living in areas with high vehicle traffic has been associated with respiratory illness	Nicolai et al. 2003; Spengler et al. 2004
	Living in areas with high vehicle traffic has been associated with exacerbation of symptoms in children and adults who already have respiratory ailments such as asthma.	Van der Zee et al. 1999; Gavett and Koren 2001
	Residence in areas with heavy vehicular traffic was linked with an increased risk of respiratory infection in early childhood and wheezing at school age	Ciccone et al. 1998
	High traffic counts in the surrounding community were not associated with increased asthma prevalence among children; however, the number of medical visits among asthmatic children increased with traffic levels, suggesting that exhaust pollutants may contribute to asthma exacerbation	English et al. 1999

HOUSING & NEIGHBORHOOD RISK FACTORS	STUDY DESCRIPTION/KEY FINDINGS	CITATION
Noise		
Crime rates, violence, neighborhood safety	Inner-city children were at great risk for exposure to violence and increased exposure was associated with asthma morbidity	Wright et al. 2004
Recreational facilities, playground equipment		
Pedestrian and bicycle access		
Water hazards		
BEHAVIORAL & SES RISK FACTORS		
SES mediators	Residence in low-income, urban areas has been implicated as an important risk factor for asthma for all children	Aligne et al. 2000; Krieger et al. 2000; Brugge et al. 2003; Litonjua et al. 1999
	There are disproportionately high rates of increased asthma incidence among children and African-Americans in the United States	Eggleston 2000
	A large portion of the observed racial and ethnic differences in asthma prevalence is explained by factors related to income and education	Litonjua et al. 1999
	Race and SES were independent and significant predictors of sensitization to cockroach allergens, regardless of whether the residence was located in an urban or suburban environment	Sarpong et al. 1996
	A majority of the variability in health status with SES can be explained by differential (and cumulative) exposures to individual environmental conditions such as hazardous wastes and other toxins, ambient and indoor air pollution, water quality, crowding, and ambient noise, as well as the physical quality of specific settings such as the home, school, work environment, and neighborhood	Evans and Kantrowitz 2002
Other behavioral factors	Evidence exists to support a causal relationship between ETS exposure and asthma exacerbation, and ETS exposure and asthma development in preschool aged children	NAS 2000
	ETS is the most harmful and ubiquitous of environmental exposures to children, and is associated with reduced lung growth, childhood asthma, respiratory tract infections, and other non-respiratory illnesses	DiFranza et al. 2004
	Females (but not males) who become overweight or obese between the ages of 6 and 11 have an increased risk of developing new asthma symptoms and increased bronchial responsiveness during the early adolescent period	Castro-Rodriguez et al. 2001
	The risk of new-onset asthma over the course of the study was higher among children who were overweight	Gilliland et al. 2003

As can be seen from Table 3.4-1, a substantial body of research exists on the relationships between asthma/respiratory outcomes and biological exposures (bioaerosols such as allergens, molds, endotoxins, etc.) in particular. Other risk factors for asthma were also investigated in the literature, although not as extensively as biological factors, including direct exposures to various chemicals (indoor and outdoor air pollution). Structural/physical housing factors and neighborhood characteristics that are hypothesized to indirectly relate to biological and chemical exposures of concern (e.g., moisture, deteriorated housing, traffic, etc.) were also the focus of numerous studies. For example, housing type and condition were related in several studies to allergen levels, and the literature also includes numerous investigations of moisture, type of heating, ventilation, and air conditioning (HVAC) system, and cleanliness as physical housing characteristics related to asthma exposures of concern. There is also a significant amount of relatively recent literature investigating the relationships between endotoxins and asthma, as well as other infections and asthma (i.e., the hygiene hypothesis) and various housing characteristics.

A limited amount of literature was identified regarding linkages between housing related viral infections and asthma. A limited number of articles regarding asthma and maternal stress during pregnancy were also found; these included one investigation of infection-related stress during pregnancy and one study on general neighborhood stressors such as crime.
The following sections detail the literature found on specific housing-related physical, chemical, and biological risk factors for asthma, as well as neighborhood and behavioral variables that may impact respiratory health. Though these factors will be discussed individually, it is important to understand the interrelationships between them to fully understand asthma risk.

3.4.3 Structural/Physical Risk Factors Related to Asthma/Respiratory Outcomes

Numerous studies have examined the relationships between structural or physical housing characteristics and respiratory health. Physical housing characteristics do not directly impact a person's risk of developing asthma but instead may indirectly affect asthma risk by promoting conditions in which biological or chemical exposures are more likely to occur.

Type of Housing. At the broadest level, factors related to housing type and age may play a role in determining asthma risk. These factors include the number of units in a given housing structure and the degree of crowding within each unit. For example, the literature indicates that cockroach allergens are generally more likely to be found at higher levels in multi-family homes, often in high-poverty regions of large metropolitan areas (Kitch et al., 2000; Arruda et al., 2001). Leaderer et al. (2002) found that residence in densely populated areas also increased the likelihood of elevated cockroach allergen levels in the home. For mouse allergen, Chew et al. (2003) observed a significant association between mouse allergen concentrations and building type, but with higher levels detected in apartment buildings having fewer than eight floors. The first National Survey of Lead and Allergens in Housing found high concentrations of mouse allergen to be most common in mobile homes, high-rise apartments, duplex or triplex buildings, and homes built prior to 1945 (Cohn et al., 2004).

Chew et al. (1999) attempted to compare the relative effects of several factors on concentrations of common indoor allergens, including housing type and seasonal variations. The authors observed that dust mite allergen concentrations were 1.9-2.4 times higher in the autumn than in the spring but that the levels in beds in single-dwelling houses were 19-31 times higher than in apartments, far outweighing the seasonal effects observed and thus underscoring the impact of housing type.

In a study of the effects of household crowding on the respiratory health of young children living in the city of Sao Paulo, Brazil, Cardoso et al. (2004) found that crowding appeared to be associated with a 60% reduction in the incidence of asthma and a 2 1/2-fold increase in the incidence of lower respiratory tract infections. Thus, the authors suggest that household crowding places young children at risk of acute lower respiratory infection but may protect against asthma, which is consistent with the hygiene hypothesis discussed in Section 3.4.5.

Housing Condition. Another structural variable with the potential to impact respiratory health is overall housing condition. Deteriorated housing (e.g., holes in floors, ceilings, and/or walls, water damage) can provide multiple access points for rodent and insect pests. Chew et al. (1999) observed a significant association between high levels of mouse allergen in inner-city

apartments and the presence of holes in walls or ceilings. Several studies have found that the level of cockroach allergen measured within housing units is also strongly associated with the degree of dwelling disrepair (measured by the presence and number of physical housing problems) in the inner-city (Chew et al., 2003; Rauh et al., 2002). In addition, pest allergens may be an important factor in asthma exacerbation in any area where deteriorated or substandard housing permits infestation, including rural areas, suburbs, and small towns and cities across the United States (Arruda et al., 2001).

Moisture. Indoor dampness and water damage have been associated with numerous respiratory health effects in the literature, including asthma, allergic symptoms, wheeze, cough, and other respiratory symptoms (Garrett et al., 1998; Kilpelainen et al., 2001; Li and Kendrick, 1995; Spengler et al., 2004). For example, in a survey of 10,667 students aged 18-25 years in Finland, Kilpelainen et al. (2001) found the risk of current asthma, allergic rhinitis, and atopic dermatitis to be higher in damp homes with visible mold, damp stains, or water damage, after adjusting for parental education, active and passive smoking, type and place of residence, pets, and wall to wall carpets. Of the respiratory infections, the risk of common colds was most clearly increased. Recent literature reviews conducted by multidisciplinary teams in Europe (EUROEXPO) (Bornehag et al., 2004) and under the National Academy of Sciences (NAS) Institute of Medicine (IOM) (NAS, 2004) in the U.S. have also found that a large body of evidence exists to link indoor dampness with respiratory health effects, though the relative effects of dampness or particular dampness-related agents (e.g., fungi, bacteria, dust mites, organic chemicals from degraded construction materials, etc.) are not yet well understood. Findings of the IOM review of the literature through late 2003 are presented in Table 3.4-2 below.

Table3.4-2. Summary of Institute of Medicine 2003 Findings Regarding the Association between Exposure to Damp Indoor Environments and Respiratory Health Outcomes [a]

Sufficient Evidence of a Causal Relationship [1]
No outcome met this definition
Sufficient Evidence of an Association [2]
Upper respiratory (nasal and throat) tract symptoms Wheeze Cough Asthma symptoms in sensitized asthmatic persons
Limited or Suggestive Evidence of an Association [3]
Dyspnea (shortness of breath) Asthma development Lower respiratory illness in otherwise healthy children
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists [4]

Airflow obstruction (in otherwise healthy persons)
Mucous membrane irritation syndrome
Chronic obstructive pulmonary disease
Inhalation fevers (nonoccupational exposures)
Lower respiratory illness in otherwise healthy adults
Acute idiopathic pulmonary hemorrhage in infants

Adapted from: NAS. 2004. Damp Indoor Spaces and Health. National Academy of Sciences Institute of Medicine.

[a] These conclusions are not applicable to immunocompromised persons, who are at increased risk for fungal colonization or opportunistic infections.

[1] Evidence fulfills the criteria for "sufficient evidence of an association" and, in addition, satisfies the following criteria: strength of association, biologic gradient, consistency of association, biologic plausibility and coherence, and temporally correct association.

[2] Evidence is sufficient to conclude that there is an association (association between the agent and the outcome has been observed in studies in which chance, bias, and confounding can be ruled out with reasonable confidence).

[3] Evidence is suggestive of an association between the agent and the outcome but is limited because chance, bias, and confounding cannot be ruled out with confidence.

[4] The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence of an association. Alternatively, no studies exist that examine the relationship.

Regarding their findings associated with asthma, the IOM committee notes that it is not clear whether these associations reflect exposures to fungi or bacteria or their constituents and emissions, to other exposures related to damp indoor environments (e.g., dust mites, cockroaches), or to some combination thereof. They suggest that the responsible factors may vary among individuals. Despite the fact that the underlying mechanisms for the association between home dampness and adverse respiratory outcomes have not been confirmed, the presence of excessive moisture or water leaks in a home has been linked to numerous asthma risk factors, including mold, dust mites, and pests.

Although the primary risk factors for home dampness can differ across climates, geographic area, and building types, features of houses that have been associated with increased moisture levels include lack of central heating, low temperatures, below-grade spaces or being on the ground floor level, poor ventilation, excess production of water in the house (e.g., humidifiers, unvented cooking), presence of pets, and water leakage or flooding (NAS, 2004). In addition, the IOM review of the literature on home dampness (NAS, 2004) noted that home dampness problems generally appear to increase as buildings age and deteriorate; however, some modern construction techniques and materials and the presence of air-conditioning have also been observed to increase the risk of dampness problems. For example, Emenius et al. (2004) followed a birth cohort of 4,089 children in Stockholm during their first two years of life to examine the impact of building characteristics on recurrent wheezing in infants. The study results indicated that relatively new apartment buildings and single-family homes with crawl space/concrete slab foundations, elevated indoor humidity, and reported wintertime windowpane condensation were associated with recurrent wheezing in infants.

Moisture level is among the most important factors affecting mold growth in homes. Most molds require fairly wet conditions (near saturation), lasting for many days, to extensively colonize an environment (NAS, 2000), though Li and Kendrick (1995) consistently observed increased levels of airborne fungi when residential water problems lasted beyond just three days. Garrett et al. (1998) attempted to identify associations between measures of house dampness, levels of airborne fungal spores, housing factors, and health outcomes in children. Investigations of 80 households, including detailed dwelling characterizations (via questionnaires and inspection surveys) and air sampling, indicated that musty odor, water intrusion, high indoor

humidity, limited ventilation through open windows, few extractor fans, and failure to remove visible indoor mold growth were associated with large airborne fungal spore concentrations. Results also suggested that these linkages may depend on the species of mold being investigated; for example, visible mold growth or condensation evidence was associated with large concentrations of *Cladosporium* spores, but not with large total spore concentrations. The authors noted, however, that actual measurements of fungal spores predicted health outcomes better than reported dampness.

To test the validity of questionnaire-based surveys on home characteristics commonly used to indicate the presence of indoor mold, Dales et al. (1997) compared survey results with dust samples measured for viable fungi and air samples for ergosterol (a component of fungal membranes). Results of this comparison showed that although reported mold, water damage, and moldy odors were associated with elevated levels of indoor fungi, inaccuracy was high. The authors suggest that research is needed to develop accurate questionnaires capable of predicting home fungal levels from home dampness characteristics, and recommend that objective measures be used in home assessments of fungi rather than questionnaires. Ren et al. (2001) also observed that surrogate measures of fungal presence in the home, such as damp spots, water damage, or leakage, as reported by household questionnaires, were not significantly and consistently related to the presence of fungal propagules measured in indoor air.

Other potential respiratory health risk factors associated with indoor moisture include dust mite levels and pests. For example, Peterson et al. (2003) found a positive association between indoor relative humidity and dust mite allergen levels. Humidity is generally accepted to be a limiting factor in dust mite growth (NAS, 2000). Arlian et al. (2001) successfully used air conditioning and dehumidifiers to reduce dust mite and allergen concentrations in homes in a temperate climate during the summer season. The humidity in a home may also be an important factor in cockroach infestations for some species. For instance, the German and American cockroaches tend to aggregate in warm, humid crevices such as those around water heaters, laundries, bathrooms, appliances, and plumbing fixtures, and the Oriental cockroach prefers damp areas such as basements, plumbing, and sewers (Eggleston and Arruda, 2001). Concentrations of cockroach allergen are typically highest in kitchens and bathrooms (i.e., where food and water sources are plentiful) (NAS, 2000; Eggleston and Arruda, 2001). Adding to the pest problem, high mouse allergen levels have been associated with cockroach infestation (Phipatanakul et al., 2000a). Both types of pests have similar environmental requirements (e.g., means of access to the home, food, and water).

Additional information on fungi, dust mites, pests, and related respiratory health effects is included in Section 3.4.5.

Building Materials and Appliances. Materials and equipment used in the home may pose a risk for asthma and other respiratory ailments. Some studies have linked chemicals used in construction materials or emitted by household appliances with asthma symptoms. These chemicals, which include volatile organic compounds (VOCs), carbon monoxide (CO), and formaldehyde, will be discussed in relation to respiratory health in Section 3.4.4.

A study by Jaakkola et al. (1999) provided new evidence of the role of polyvinyl chloride (PVC) plastics and textile wall materials in the development of bronchial obstruction in young children. Observations of a cohort of 3,754 newborns in Oslo, Norway for the first two years of life indicated that the risk of bronchial obstruction was related to the presence of PVC flooring and textile wall materials relative to wood or parquet flooring and painted walls and ceiling. Further analysis revealed an exposure-response relationship between the assessed amount of PVC and other plasticizer-containing surface materials and the risk of bronchial obstruction. In a later study of 2,568 children aged one to seven in Finland, Jaakkola et al. (2000) found evidence that emissions from plastic wall materials indoors may have adverse effects on the lower (but not upper) respiratory tracts of small children, including symptoms such as persistent wheezing, cough, and phlegm. The risks of asthma and pneumonia also appeared to increase in children exposed to such materials. In a cross-sectional study of 5,951 Russian children aged eight to twelve (Jaakkola et al., 2004), new linoleum flooring, synthetic carpeting, particleboard, wall coverings, furniture type, and recent painting were observed to be additional determinants of risks of current asthma, wheezing, and allergy.

Heating, Ventilation, and Air Conditioning (HVAC) Systems. Equipment used for heating, ventilation, and air conditioning (HVAC) may influence the development of allergies and asthma in the home. HVAC equipment can increase or decrease humidity levels, and increased humidity levels promote mold and mildew growth and dust mite proliferation. The potential for air conditioners to reduce indoor allergen levels was noted by van Strein et al. (2004), who found a consistent relationship between the absence of air conditioning and increased dust mite allergen concentrations, though these increases were not dramatic (no greater than a factor of two).

The use of forced air heating systems was inversely related to dust mite allergen and airborne fungi concentrations in several studies (Li and Kendrick, 1995; Arbes et al., 2003; Peterson et al., 2003). Li and Kendrick (1995) found that reports of allergic symptoms by residents of homes with forced air heating systems, air filters, air conditioners, and humidifiers installed within the furnace (which have the potential to filter out mold spores) were significantly less severe than average. However, Hirsch et al. (2000) observed that the installation of central heating systems and insulated windows was associated with increased dust mite allergen and mold spore concentrations.

Oie et al. (1999) (in a companion study to Jaakkola et al., 1999) assessed the role of ventilation rate in homes in the development of bronchial obstruction during the first two years of life in a cohort of 3,754 newborns in Oslo. Ventilation rate and other building characteristics were collected through home visits, and questionnaires were used to obtain additional information. Results of the study indicated that although ventilation rate itself was not directly associated with bronchial obstruction, low ventilation rates did strengthen the effects of indoor air pollutants (e.g., environmental tobacco smoke, plasticizers) that increased bronchial obstruction risks. Emenius et al. (2004) also found that air change rate and type of ventilation system in the home did not seem to directly affect the risk of recurrent wheezing in infants, in a birth cohort study of 4,089 children in Stockholm during their first two years of life.

Home Cleanliness. Some of the variables described above may be beyond a resident's control, such as housing type or the quality of HVAC equipment installed in rental units, but one physical housing characteristic with implications for respiratory health is primarily dependent on the actions of those living within the residence: cleanliness. This risk factor is multi-faceted, as it encompasses general housekeeping, as well as the condition of materials that may promote allergen exposure and the presence of bacteria in an otherwise tidy home. Lack of sufficient cleaning, excess clutter, and failure to properly store food items may attract cockroaches, a common allergen in inner-city environments (Kattan et al., 1997). Inadequate cleaning may also promote an overabundance of dust mites and animal dander. Everyday items common to many households, such as upholstered furniture, carpeting, and draperies, act as reservoirs for allergenic proteins from dust mites, insects, and pets. Endotoxins, which are cell wall components of bacteria that have been associated with asthma symptoms (see additional discussion in section 3.4.5), are ubiquitous in nature and are normally found indoors as components of house dust (Gehring et al., 2004).

Home Furnishings. Certain home furnishing may have the potential to influence indoor air quality, including through direct release of chemicals, by providing a favorable environment for allergen or mold proliferation, or by serving as a reservoir for dust that contains both chemicals and allergens (also see discussion on "Home Cleanliness" above).

For example, molds can obtain nutrients and moisture sufficient for growth from water-affected building materials such as glues used to bond carpet to its backing. Li and Kendrick (1995) found that overall fungal levels (as assessed by counting spores in environmental samples) increased with the presence of damp conditions and carpets.

Some of the primary determinants of dust mite growth in homes can also be the availability of upholstered furniture, carpeting, mattresses, and pillows (in addition to temperature and humidity) (Vaughan and Platts-Mills, 2000). In response to a previous study of homes in New Zealand that found carpets on floors were the most important determinants of floor dust mite allergen levels, Wickens et al. (2001) attempted to determine to what extent housing characteristics might explain observed variability in dust mite allergen levels between houses. Study results showed that houses with insulation or a room or garage below the living room had approximately half the dust mite allergen concentration than houses without these features. Carpet underlay less than 8 mm thick was also associated with an almost 3-fold increase in dust mite allergen levels when compared with thicker carpet underlays. The authors suggested that the most important housing characteristic explaining the between-house variability in mite allergen levels on carpeted living room floors was the presence of insulated floors.

In contrast, Chew et al. (1998) evaluated the usefulness of a home characteristics questionnaire in predicting indoor allergen levels and found that although certain home characteristics (such as smooth versus carpeted floors) were significant predictors of increased allergen levels, home characteristics reporting was a relatively weak predictor of the absence of allergen. For example, in comparison to dust from smooth floors, dust from carpeted bedroom floors had 2.1 times the risk of having dust mite allergen at levels ≥ 10 μg/g; however, high levels of allergen were also measured in situations where no carpets were present. The authors noted that relatively high levels of allergens can be present even in situations where general home characteristic would

suggest otherwise (e.g., where beds were encased in plastic, no cats were present, no carpets were present, and no sign of cockroaches had been reported).

Cleaning practices used on carpets have also been shown to influence allergen and endotoxin levels. For example, Wickens et al. (2003) looked at the relationship between carpets and endotoxin distribution in house dust, and observed increases in endotoxin levels following steam cleaning or shampooing the carpet, presumably due to increases in relative humidity of the carpet. Endotoxins are bacterial components which have been shown to be associated with asthma severity. Vojta et al. (2001) observed that both vacuuming plus dry steam cleaning and vacuuming alone resulted in significant reductions in dust mite allergen concentrations and loads in carpets. Furthermore, reductions in carpet mite allergen levels persisted longer with the vacuuming plus steam cleaning than for the vacuuming alone (e.g., 8 weeks versus 4 weeks). However, steam cleaning may also increase moisture levels in the carpet, thus leading to eventual increased dust mite and mold proliferation.

As discussed above, certain home furnishings such as carpets or textile wall coverings can also contribute to degraded indoor air quality through off-gassing of chemicals (Jaakkola et al., 2004). For example, new carpets and furniture can be a potential source of formaldehyde, which has been linked to respiratory symptoms (Garrett et al., 1999; Godish and Rouch, 1987). These chemical risk factors are discussed in further details below.

3.4.4 Chemical Risk Factors Related to Asthma/Respiratory Outcomes

Although the body of evidence regarding respiratory symptoms and exposure to chemical agents is primarily based on data from occupational settings with much higher level exposures than found in residential settings, limited research has suggested that indoor exposure to formaldehyde and certain other volatile organic compounds (VOCs), some household products such as pesticides, and various combustion by-products (nitrogen oxides) can be related to asthmatic symptoms in susceptible individuals (Becher et al., 1996; Garrett et al., 1999).

In support of the U.S. Environmental Protection Agency's (EPA) efforts to develop an asthma outreach strategy, the National Academies' of Science (NAS) Institute of Medicine (IOM) conducted a review of available data on asthma and indoor air exposures published in the literature through 1999 (NAS, 2000). In this 1999 IOM assessment, a number of chemical and biological exposures in the home were categorized according to the strength of their relationship with asthma development and/or exacerbation, as based on a uniform set of criteria regarding sufficiency of evidence. Table 3.4-3 summarizes general findings and conclusions of the IOM assessment committee regarding the association between indoor exposure to chemical agents and asthma development and exacerbation.

Table 3.4-3. Summary of IOM 1999 Findings Regarding the Association Between Chemical Exposures in the Home and the Development and Exacerbation of Asthma in Sensitive Individuals.

Development of Asthma	Exacerbation of Asthma
Sufficient Evidence of a Causal Relationship [1]	
No agents met this definition	ETS (in preschool-aged children)
Sufficient Evidence of an Association [2]	
ETS (in preschool-aged children)	Nitrogen oxides (high-level exposures)[3]
Limited or Suggestive Evidence of an Association [4]	
No agents met this definition	ETS (in older children and adults) Formaldehyde Fragrances
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists [5]	
Nitrogen oxides Pesticides Plasticizers VOCs Formaldehyde Fragrances ETS (in older children and adults)	Pesticides Plasticizers VOCs
Limited or Suggestive Evidence of No Association [6]	
No agents met this definition	No agents met this definition

Adapted from: NAS. 2000. Clearing the Air: Asthma and Indoor Air Exposures. National Academy of Sciences Institute of Medicine.

[1] Evidence fulfills association criteria and in addition satisfies criteria regarding the strength of association, biologic gradient (dose-response effect), consistency of association, biologic plausibility and coherence, and temporality used to assess causality.

[2] Association has been observed in studies in which chance, bias, and confounding factors can be ruled out with reasonable confidence (e.g. several small bias free studies showing an association that is consistent in magnitude and direction

[3] At concentrations that may occur only when gas appliances are used in poorly ventilated kitchens

[4] Evidence is suggestive of an association but is limited because chance, bias, and confounding cannot be ruled out with confidence (e.g., one high quality study shows association, but results of other studies are inconsistent)

[5] Available studies are of insufficient quality, consistency, or statistical power to permit a conclusion; or no studies exist

[6] Several adequate studies are mutually consistent in not showing an association (but limited to the conditions, level of exposure, and length of observation covered in the study).

In the National Academies' IOM review of the available literature through 1999, no indoor chemical exposures were conclusively linked with asthma development. However, sufficient evidence of a causal relationship between environmental tobacco smoke (ETS) exposure and asthma exacerbation was found. ETS exposure was also found to be associated with asthma development in preschool aged children, and limited evidence of an association was observed between ETS exposure and asthma exacerbation in adults and older children. Because exposure to ETS is determined in large part by residential behavior, further discussion of this risk factor is included in Section 3.4.7: Behavioral and Socioeconomic Factors Related to Asthma/Respiratory Outcomes.

Organic Chemicals. The NAS review found limited evidence regarding an association between formaldehyde and fragrance exposures and asthma exacerbation, and inadequate or insufficient evidence for determination of the exact role of other indoor pollutants, such as pesticides and VOCs, in asthma exacerbation or development (NAS, 2000). Other research in Sweden has reported a significant association between elevated indoor formaldehyde and VOC

concentrations and asthmatic symptoms (Norback et al., 1995), and a strong relationship was found between formaldehyde concentration and exacerbation of wheezing illness in a recent U.K. study (Venn et al., 2003). Formaldehyde and VOC emissions were also associated with airway inflammation in a European study (Wieslander et al., 1997).

Common indoor sources of formaldehyde reported in the literature include particle board (e.g., applied as subflooring), plywood, wood paneling, urea foam insulation, and some carpets, furniture, and upholstery fabrics (Garrett et al., 1999; Godish and Rouch, 1987; Wiglusz et al., 1991). Certain types of paint can also be sources of formaldehyde and VOC emissions (Wieslander et al., 1997). Jaakkola et al. (2004) also observed risks of current asthma, wheezing, and allergy to be related to recent renovation and the installation of materials with potential chemical emissions, including new linoleum flooring, synthetic carpeting, particleboard, wall coverings, and recent painting.

Releases from formaldehyde-containing materials and furnishings, such as fabrics and composite building materials like particle board that are constructed with urea-formaldehyde resins, have been observed to increase with the humidity and temperature of the surrounding air, as well as age of the product (Godish and Rouch, 1986; NAS, 2004; Wiglusz et al., 1990; Wiglusz et al., 1991; Wiglusz et al., 1995). For example, Godish and Rouch (1986) studied the effect of indoor climate control on mitigation of formaldehyde contamination in mobile homes, using nine indoor climate regimes. Analysis of formaldehyde levels in indoor air, temperature, and relative humidity (RH) ranges showed that reducing temperature and humidity levels significantly reduced formaldehyde levels in the home. A reduction in temperature alone from 30 degrees Celsius (C) to 20 degrees C (approximately 86 F to 68 F) resulted in an approximate 70 percent reduction in formaldehyde levels in indoor air, and a reduction in relative humidity alone from 70 percent to 30 percent resulted in an approximate 40 percent reduction in formaldehyde levels. Looking at the combined effects of temperature and humidity, formaldehyde levels were reduced by 80 percent at the lowest combination of temperature and relative humidity (20 degrees C, 30 percent RH) compared to levels measured at the highest combination of temperature and relative humidity (30 degrees C, 70 percent RH). Wiglusz et al. (1991) conducted a laboratory study to investigate the rates of formaldehyde release from fabrics used in furniture upholstery and window drapes as a function of textile age, indoor air temperature, and home relative humidity. Results of the study showed that although responses varied with each fabric tested, increases in temperature and humidity generally increased formaldehyde emissions from the fabrics, and that these fabrics may serve as an indoor air source of formaldehyde for many months.

Pesticides. Although there is currently no conclusive evidence of a link to indoor exposure to pesticides and exacerbation of childhood asthma, associations have been observed between asthma/airway constriction and pesticide exposure in adults in occupational settings (Etzel, 1995; CDC, 2003). Contaminants such as odor-producing agents in organophosphate pesticides have been linked to asthma in adults; these agents are thought to be low-molecular weight mercaptans and sulphides (Quarles, 1999; O'Malley, 1997). Pyrethroid pesticides applied via ground spraying to neighborhoods for West Nile virus vector (mosquito) control have also been linked to asthma in case reports from New York City in 2000 (CDC, 2003). However, in a comprehensive data analysis, Karpati et al. (2004) was not able to find any population-level increases in public hospital emergency room visit rates for asthma as a result of pesticide spraying in New York in

2000. However, because studies indicate that exposure to organophosphate pesticides disrupts the part of the nervous system that regulates the motor functioning of the lungs, some researchers also hypothesize that pesticides may be related to the occurrence of asthma in children (Eskenazi et al., 1999). Thus, while insect and rodent infestation may be important asthma triggers, the pesticides being used to fight infestations can also create exposure hazards (Bashir, 2002).

Which children are most at risk for pesticide exposure is unclear. Those living in agricultural areas may be exposed to higher pesticide levels than other children because of pesticides tracked into their homes by household members, by pesticide drift, or by playing in nearby fields (Eskenazi et al., 1999), while other research indicates that pesticides are of particular concern in low-income, inner-city areas, where conditions favor pest infestation and, consequently, pesticide usage (Berkowitz et al., 2003). As concerns with pesticide exposures are predominantly associated with children's neurobehavioral and neurodevelopmental outcomes, detailed information on pesticide use and storage patterns in the home, as well as additional adverse health effects for children, is included in Section 3.2.4 of this report.

Combustion By-Products. Combustion by-products have also been linked in the literature to asthma-related symptoms. In particular, high-level, short-term exposure to nitrogen dioxide, which occurs as a result of poorly ventilated kitchens or the use of a gas appliance for heating purposes, may be particularly detrimental to asthmatic individuals (NAS, 2000). In a study of 768 infants at risk for developing asthma, Van Strein et al. (2004) found that infants living in homes with an NO_2 concentration exceeding 17.4 ppb had a higher frequency of days with wheeze, persistent cough, and shortness of breath when compared with infants in homes that had NO_2 concentrations lower than 5.1 ppb. The National Ambient Air Quality Standard for Nitrogen Dioxide in the U.S. is currently 53 ppb (annual arithmetic mean). Chauhan et al. (2003) also uncovered an association between nitrogen dioxide exposure and the intensity of virus-induced asthma exacerbation in children. Indoor nitrogen dioxide sources and levels were characterized by Garrett et al. (1999) in an Australian study of 80 homes. Passive samples collected on five occasions over one year showed that mean indoor levels were higher than outdoor levels, and varied with season (with highest levels recorded in the winter). The overall median level was 6.0 ppb, ranging up to 128 ppb. The major indoor nitrogen dioxide sources observed by the authors were: gas stoves, vented gas heaters, and smoking, with gas stoves being the main contributors.

A cross-sectional analysis of data from the Third National Health and Nutrition Examination Survey (NHANES III) found a significant association between doctor-diagnosed asthma and the use of a gas oven or stove for heat (Lanphear et al., 2001a). An Australian study also identified gas stove use as a significant risk factor for respiratory symptoms independent of nitrogen dioxide levels, suggesting that gas stoves may present other risks apart from nitrogen dioxide emissions (Garrett et al., 1998). Wong et al. (2004) investigated the association between household gas cooking and respiratory illnesses in 426 preschool children in two housing estates with contrasting air quality in Hong Kong. The authors found that household gas cooking was positively associated with respiratory illnesses, and that there was a dose-response relation between the frequency of gas cooking and the prevalence of respiratory illnesses in the estate with lower outdoor air pollution, but not for the more polluted estate. Kilpelainen et al. (2001) also attempted to look deeper into the association between respiratory symptoms (allergic

rhinitis) and combustion appliances (wood stove heating), and found that the significant association disappeared in the multivariate analysis after adjusting for various family indoor and outdoor factors. Most importantly, childhood residential environment on a farm was observed to be the main confounding factor related to association between wood stove heating and asthma.

EPA's Air Quality Criteria for Carbon Monoxide (EPA, 2000) reviews recent research related to health effects, including asthma exacerbation, of low level exposure to another combustion gas, carbon monoxide (CO). Although CO exposure was correlated with asthma exacerbation in several of the studies, EPA concluded that the relationship between short-term low levels of CO exposure and the frequency of respiratory disease cannot yet be interpreted with confidence (EPA, 2000). In the studies reviewed by EPA, the authors hypothesized that CO may be a marker for other combustion products which exacerbate asthma (Sheppard et al., 1999; Norris et al., 1999).

Additional information on housing characteristics associated with carbon monoxide/combustion by-products was discussed in Section 3.3.4 on injury.

3.4.5 Biological Risk Factors Related to Asthma/Respiratory Outcomes

In contrast to the relatively modest amount of information available on indoor chemical exposures and asthma, a significant amount of research has been conducted on the relationship between asthma and biological risk factors in the home. Hypothesized biological risk factors for asthma identified in the literature include multiple allergen sources, such as dust mites, fungi, and pets, as well as microbial organisms and viruses. Epidemiologic studies have demonstrated a strong association between exposure to indoor allergens and allergic sensitization, which could potentially lead to asthma and other respiratory symptoms in children and young adults who are genetically susceptible to such ailments (Arshad, 2003; Finn et al., 2000; Gold, 2000). Evidence suggests that sensitization occurs at different exposure levels for various allergens (Murray et al., 2001) and that exposure to slightly elevated levels of multiple allergens may have an even greater effect on respiratory symptoms than exposure to very high levels of just one allergen (Gehring et al., 2001). In an attempt to quantify the contribution of indoor allergens to asthma in U.S. children and adolescents, Lanphear et al. (2001b) suggested that nearly 45% of doctor-diagnosed asthma could be attributed to residential risk factors such as dust mite, cockroach, and pet allergens.

As discussed in Section 3.4.4, in 1999 the NAS reviewed available research on the relationship between indoor air exposures and asthma (NAS, 2000). Table 3.4-4 summarizes the conclusions of the assessment committee regarding the association between indoor exposure to biological agents and asthma development and exacerbation. Following the table, key studies relevant to the specific biological agents primarily associated with asthma are discussed further.

Table 3.4-4. Summary of NAS Findings Regarding the Association Between Biological Exposures in the Home and the Development and Exacerbation of Asthma in Sensitive Individuals.

Development of Asthma	Exacerbation of Asthma
Sufficient Evidence of a Causal Relationship [1]	
Dust mite	Cat Cockroach Dust mite
Sufficient Evidence of an Association [2]	
No agents met this definition	Dog Fungi or mold [a] Rhinovirus
Limited or Suggestive Evidence of an Association [3]	
Cockroach (in preschool-aged children) Respiratory Syncytial virus	Domestic birds *Chlamydia pneumoniae* *Mycoplasma pneumoniae* Respiratory Syncytial virus
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists [4]	
Cat, Dog, Domestic Birds Rodents Cockroaches (except for preschool-aged children) Endotoxins Fungi or molds *Chlamydia pneumoniae* *Mycoplasma pneumoniae* *Chlamydia trachomatis* Houseplants Pollen	Rodents [5] *Chlamydia trachomatis* Endotoxins Houseplants Pollen Insects other than cockroaches
Limited or Suggestive Evidence of No Association [6]	
Rhinovirus	No agents met this definition

Adapted from: NAS. 2000. Clearing the Air: Asthma and Indoor Air Exposures. National Academy of Sciences Institute of Medicine.

[a] Also see IOM 2003 literature review (NAS, 2004; discussed below) on damp indoor spaces/mold and health effects.

[1] Sufficient Evidence of a Causal Relationship: Evidence fulfills association criteria and in addition satisfies criteria regarding the strength of association, biologic gradient (dose-response effect), consistency of association, biologic plausibility and coherence, and temporality used to assess causality.

[2] Sufficient Evidence of an Association: Association has been observed in studies in which chance, bias, and confounding factors can be ruled out with reasonable confidence (e.g. several small bias free studies showing an association that is consistent in magnitude and direction

[3] Limited or Suggestive Evidence of an Association: Evidence is suggestive of an association but is limited because chance, bias, and confounding cannot be ruled out with confidence (e.g., one high quality study shows association, but results of other studies are inconsistent)

[4] Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists: Available studies are of insufficient quality, consistency, or statistical power to permit a conclusion; or no studies exist

[5] Since the time of the NAS review and assessment, analysis of a subset of data from the National Inner-City Asthma Study indicates that mouse allergens may be an important indoor allergen in inner-city children with asthma, with exposure and hereditary disposition being risk factors contributing to mouse sensitization (Phipatanakul, 2000a and 2000b).

[6] Limited or Suggestive Evidence of No Association: Several adequate studies are mutually consistent in not showing an association (but limited to the conditions, level of exposure, and length of observation covered in the study).

Dust Mites. At this time, house dust mites are the only home allergen source for which the IOM 1999 review found sufficient evidence in the literature of a causal relationship between exposure and the development of asthma in susceptible children. Evidence supporting an association between exposure to dust mite allergens and asthma exacerbation is also well

documented in the general literature (NAS, 2000; Custovic et al., 1998; Platts-Mills et al., 1997). In a review of studies on middle-class or mixed economic-class asthmatic children, Kattan et al. (1997) reported that 50-60% of children had positive skin test results to dust mites. Based on results from a national survey, Arbes et al. (2003) concluded that over 80% of U.S. homes have detectable levels of house dust mite allergen in the bedroom and that allergen levels associated with allergic sensitization and asthma exacerbation are common. Wahn et al. (1997) found that children with a family history of allergic sensitization are particularly susceptible to even very low levels of exposure to dust mites and other indoor allergens.

Mites are a very common exposure source in temperate and humid regions such as the southeastern United States. Some of the major mite allergens identified and isolated to date include those from *Dermatophagoides farinae* (Der f 1, 2, 3, 5, 7, and 10), *D. pteronyssinus* (Der p 1), and *Blomia tropicalis* (Blo t 5). *Dermatophagoides farinae*, *D. pteronyssinus*, and other *Dermatophagoides* species comprise most of the mite species present in U.S. homes, although *Blomia tropicalis* may also be common in the southern states of the U.S. (Curtis et al., 1997). Most dust mite exposure is thought to occur as mite fecal pellets and aggregates associated with larger (~10-25 μm) dust particles become airborne during and immediately after disturbance of dust reservoirs (NAS, 2000).

The primary determinants of dust mite growth in homes are food source (i.e., skin scales), temperature, humidity and the availability of upholstered furniture, carpeting, mattresses, and pillows (Vaughan and Platts-Mills, 2000). Of these, humidity is generally the limiting factor (NAS, 2000). The critical humidity level for mite survival is temperature dependent and ranges from 55% to 73% for temperatures between 15°C and 35°C (Arlian, et al., 2001). Other features of houses that can increase levels of mite growth include poor ventilation, excess production of water in the house (e.g., humidifiers, unvented cooking), water leakage, poor cleaning habits, and being on the ground floor level (NAS, 2000). Several studies have also reported a positive relationship between family size and mite allergen levels (Peterson et al., 2003; Wickens et al., 2001). A New Zealand study detected a strong association between the presence of floor insulation and lower dust mite allergen levels, though the authors were unable to conclusively identify the reason for this association (Wickens et al., 2001).

Despite the conclusions of the IOM 1999 review, questions remain about asthma sensitization and exacerbation exposure levels for dust mite allergens. Sporik et al. (1990) reported that exposures during infancy to dust mite allergen concentrations above 2 μg/g and 10μg/g of house dust were associated with sensitization and exacerbations, respectively, while results from the Childhood Allergy Study found that although house dust mite sensitization and asthma were related, no relationship between level of dust mite allergen exposure in children's bedrooms in early childhood and development of asthma was found (Carter et al., 2003).

Cockroaches. Although over 50 cockroach species occur in the U.S., only five species are commonly found in residential settings: the German Cockroach (*Blatella germanica*), the American Cockroach (*Periplaneta americana*), the Oriental Cockroach (*Blatta orientalis*), the Smoky Brown Cockroach (*Periplaneta fuliginosa*), and the Brown-banded Cockroach (*Supella Longipalpus*) (Eggleston and Arruda, 2001). Some of the major cockroach allergens identified and isolated to date include those from *Blatella germanica* (Bla g 1 and Bla g 2) and *Periplaneta*

americana (Per a 3). Sources of cockroach allergen include body parts, the GI tract, saliva, and feces. Like house dust mite allergens, cockroach allergens are also thought to be associated with larger particles that are only airborne during and immediately after disturbances of dust reservoirs. Concentrations of cockroach allergens are typically highest in kitchens and bathrooms (i.e., where food and water sources are plentiful), although high levels have also been observed in bedrooms (NAS, 2000; Eggleston and Arruda, 2001). The humidity in a home may be an important factor in cockroach infestations for some species, such as the German and American cockroaches, which tends to aggregate in warm, humid crevices such as those around water heaters, laundries, bathrooms, appliances, and plumbing fixtures, and the Oriental cockroach, which prefers damp areas such as basements, plumbing, and sewers (Eggleston and Arruda, 2001).

The literature indicates that allergens derived from the cockroach are an important source of sensitization, particularly in areas where cockroach infestation is common (NAS, 2000; Chapman et al., 1997). Alp et al. (2001) reported that sensitization to cockroach allergens may develop earlier in childhood and be more prevalent than previously realized, noting that one study subject exhibited sensitization by six months of age. Another study tied exposure to cockroach allergens at three months of age to measurable allergic response by the age of two years (Finn et al., 2000). Other research has linked cockroach allergen exposure even more directly with asthma. For example, in an ongoing longitudinal family and birth cohort study, Litonjua et al. (2001) observed that, in comparison to children living in homes with very low levels of cockroach allergen (defined in this study as less than 0.05 Units/g dust of Bla g 1 or 2, two commonly measured cockroach allergens), children exposed to Bla g 1 or 2 levels ranging from 0.05 to less than 2 Units/g had a relative risk for doctor-diagnosed asthma of 8.27, and children exposed to Bla g 1 or 2 levels of 2 Units/g or greater had a relative risk for doctor-diagnosed asthma of 35.87. Based on these findings, the authors concluded that exposure to cockroach allergen early in life may contribute to the development of asthma in susceptible children (Litonjua et al., 2001). Recent evidence suggests that exposure to high levels of cockroach allergen may be more widespread than previously thought. Matsui et al. (2003) observed that over 40% of a middle-class, suburban study population had elevated levels of cockroach allergens in the home and that sensitization may occur at levels as low as 1 Unit/g.

Like dust mites, cockroaches thrive in temperate and humid regions but may also proliferate in northern states (Chapman et al., 1997). The literature indicates that cockroach allergens are generally more likely to be found at higher levels in multi-family homes, often in high-poverty regions of large metropolitan areas (Kitch et al., 2000; Arruda et al., 2001). This differs from single-family dwellings, in which dust mite allergens are often more likely to be the dominant allergens (Gergen, pers. comm.). In the National Cooperative Inner City Asthma study (NCICAS), cockroach allergen was the second most common sensitizer (36%) in 1,286 asthmatic children tested via skin prick tests (Kattan et al., 1997). In contrast, in their review of studies of middle-class or mixed economic-class asthmatic children, Kattan et al. (1997) report that positive skin tests to cockroach were uncommon, and were instead dominated by sensitivity to dust mites and cat or dog. Leaderer et al. (2002) observed similar results in a study of a socioeconomically diverse New England population, which found associations between low socioeconomic status, African-American or Hispanic ethnicity, low maternal education, and residence in densely populated areas with increased likelihood of elevated cockroach allergen

levels in the home. However, cockroach allergens may be an important factor in asthma exacerbation in any area where deteriorated or substandard housing permits cockroach infestation, including rural areas, suburbs, and small towns and cities across the United States (Arruda et al., 2001; Rauh et al., 2002).

Rodents. The IOM 1999 Review found evidence of an association between exposure to rodents and asthma exacerbation from occupational exposure in a laboratory setting only (NAS, 2000). However, since the time of the IOM assessment, a subset of data from the National Cooperative Inner-City Asthma Study has been analyzed, and it supports a significant association between exposure to mouse *(Mus musculus)* allergen (Mus m 1) and asthma sensitization, particularly in inner-city, multiple-family dwellings (Phipatanakul, 2000b). In this analysis, children whose homes had mouse allergen levels above the median (1.60 μg/g) in the kitchen had a significantly higher rate of mouse sensitization. Mouse allergens were also found to be widely distributed in inner-city homes, with 95% of all homes assessed having detectable mouse allergen in at least one room (Phipatanakul, 2000a). Chew et al. (2003) observed that mouse allergen was common in low income, inner-city apartments, even where sightings were not reported. Higher mouse allergen levels have also been associated with evidence of cockroach infestation in any room (Phipatanakul, 2000a). Recent evidence lends additional credence to the association between rodent allergen exposure and asthma. An investigation of inner-city homes found detectable levels of rat allergen (Rat n 1) in 33% of the dwellings assessed and observed significantly higher asthma morbidity in children sensitized to rats (Perry et al., 2003). Findley et al. (2003) also documented a strong association between the presence of rats or mice in the home and asthma, particularly among Puerto Rican residents. Finally, as part of the National Survey of Lead and Allergens in Housing, Cohn et al. (2004) analyzed dust samples taken from 831 nationally representative homes. Detectable levels of mouse allergen were found in 82% of U.S. homes.

Research on the presence of rodents in residential settings has identified several housing characteristics that increase the risk of exposure to rodent allergens. Chew et al. (2003) associated higher mouse allergen concentrations with visible holes in walls or ceilings, absence of a cat, and residential buildings with fewer than eight floors. The first National Survey of Lead and Allergens in Housing detected elevated levels of mouse allergen (>1.60 μg/g) in 82% of homes (n=831); high concentrations were most common in mobile homes, high-rise apartments, duplex or triplex buildings, and homes built prior to 1945 (Cohn et al., 2004).

Molds. There are over 200 species of fungi, including those commonly called "mold," to which people are routinely exposed indoors and outdoors (NAS, 2000).

The primary factor affecting fungal growth in homes is moisture level. In general, most molds require fairly wet conditions (near saturation), lasting for many days, to extensively colonize an environment (NAS, 2000). Molds can obtain nutrients and moisture sufficient for growth from water-affected building materials such as wood, insulation materials, cellulose in the paper backing on drywall, and glues used to bond carpet to its backing, as well as furniture, clothing, and dust and dirt. Features of houses that can increase moisture levels and fungal growth include being on the ground floor level, poor ventilation, excess production of water in the house (e.g., humidifiers, unvented cooking), and water leakage or flooding. Some of the most abundant

fungi genera found in homes without severe water damage include: *Alternaria, Cladosporium, Penicillium*, yeasts, and *Aspergillus* (Burge and Otten, 1999; American Academy of Pediatrics, 1998; Bush and Portnoy, 2001; Gravesen, 1999). Most of these molds do not typically produce toxins (mycotoxins) (Etzel, 2000), but they may be important as sources of mold allergens. In contrast, under certain very damp conditions (i.e., in the presence of water-soaked cellulosic materials), some molds may be induced to produce mycotoxins or toxin producing molds (e.g., *Stachybotrys chartarum*) may be prominent (Flannigan, 1997; Boutin-Forzano et al., 2004). In general, whether or not a potentially toxigenic fungus produces toxins is dependent on environmental conditions and nutrient source, with very damp conditions (Burge and Amman, 1999). Boutin-Forzano et al. (2004) investigated the relationship between high relative humidity within dwelling walls and growth of *Stachybotrys chartarum* and other molds in 458 samples from 100 homes. Measurements showed that mean relative wall humidity was significantly higher in areas where *Stacybotrys* was identified, compared to areas where other or no molds were identified. In addition, there was no straightforward relationship between wall humidity and room humidity.

Numerous studies support the association between mold and excess moisture, though predicting which houses will contain high concentrations of fungal spores can be complicated. Li and Kendrick (1995) found that overall fungal levels (as assessed by counting spores in environmental samples) were highest in living rooms, followed by family rooms, kitchens, bathrooms, and bedrooms. This study also observed that fungal levels increased with the presence of damp conditions and carpets and decreased where forced-air heating systems, dehumidifiers, air filters, and air conditioners were present. Various methods have been pursued to predict which children may be at risk for mold exposure, including home questionnaires and inspections for water damage and visible mold. A European study that utilized both subjective and objective markers of lung function found an association between self-reported mold and respiratory health (Andriessen et al., 1998). However, visual inspection might not be a consistent method of identifying mold problems. Ren et al. (2001) observed that surrogate measures of fungal presence in the home, such as damp spots, water damage, or leakage, as reported by household questionnaires, were not significantly and consistently related to the presence of fungal propagules measured in indoor air.

Mold exposure in homes primarily occurs as airborne spores and hyphal fragments, but molds are also present in household dust and on surfaces. Release of mold spores or fragments into indoor air is usually dependent on some sort of mechanical disturbance, although for some types of molds slight air movement may be sufficient (e.g., air movement by a fan), or spores may become airborne through natural spore discharge mechanisms. Most molds release spores ranging in size from 2 to 10 μm, although some may be released as chains or clumps of spores (NAS, 2000).

Numerous studies have linked fungal exposure with asthma and respiratory symptoms. As discussed previously, the Institute of Medicine (IOM) recently conducted a review of literature published through late 2003 focusing on indoor dampness and mold and respiratory health effects (NAS, 2004). Findings of the IOM 2003 review of the literature regarding mold exposures are presented in Table 3.4-5. below.

Table 3.4-5. Summary of IOM 2003 Findings Regarding the Association between Exposure to Mold or Other Agents in Damp Indoor Environments and Respiratory Health Outcomes [a]

Sufficient Evidence of a Causal Relationship [1]
No outcome met this definition
Sufficient Evidence of an Association [2]
Upper respiratory (nasal and throat) tract symptoms Wheeze Asthma symptoms in sensitized asthmatic persons Cough Hypersensitivity pneumonitis in susceptible persons [b]
Limited or Suggestive Evidence of an Association [3]
Lower respiratory illness in otherwise-healthy children
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists [4]
Dyspnea (shortness of breath) Airflow obstruction (in otherwise-healthy persons) Asthma development Mucous membrane irritation syndrome Chronic obstructive pulmonary disease Inhalation fevers (nonoccupational exposures) Lower respiratory illness in otherwise-healthy adults Acute idiopathic pulmonary hemorrhage in infants

Adapted from: NAS. 2004. Damp Indoor Spaces and Health. National Academy of Sciences Institute of Medicine.

[a] These conclusions are not applicable to immunocompromised persons, who are at increased risk for fungal colonization or opportunistic infections.

[b] For mold or bacteria in damp indoor environments.

[1] Evidence fulfills the criteria for "sufficient evidence of an association" and, in addition, satisfies the following criteria: strength of association, biologic gradient, consistency of association, biologic plausibility and coherence, and temporally correct association.

[2] Evidence is sufficient to conclude that there is an association (association between the agent and the outcome has been observed in studies in which chance, bias, and confounding can be ruled out with reasonable confidence).

[3] Evidence is suggestive of an association between the agent and the outcome but is limited because chance, bias, and confounding cannot be ruled out with confidence.

[4] The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence of an association. Alternatively, no studies exist that examine the relationship.

Research clearly indicates that exposure to mold plays a role in the exacerbation of asthma symptoms in sensitized individuals, although the association between mold exposure and asthma development remains undetermined (NAS, 2000). Molds are thought to play a role in asthma in several ways. They are known to produce a large number of proteins that are potentially allergenic, and there is sufficient evidence to support associations between fungal allergen exposure and asthma exacerbation and upper respiratory disease (NAS, 2000). Some of the major mold allergens identified and isolated to date include those from *Aspergillus fumigatus* (Asp f 1, 2, 6, and 12), *Alternaria alternata* (Alt a 1, 2, 3, 6, 7, and 10), and *Cladosporium herbarum* (Cla h 1, 2, and 3), as well as others such as *Aspergillus oryzae*, *Penicillium citrinum, Penicillium chrysogenum, Trichophyton tonsurans, Malassezia furfur*, and *Psilocybe cubensis* (NAS, 2000). An estimated 6-10% of the general population and 15-50% of those who are genetically susceptible (atopic) are sensitized to mold allergens (NAS, 2000). In addition, molds may play a role in asthma via release of irritants that increase potential for sensitization, or release of toxins that affect immune response (NAS, 2000).

Reflecting differences in specific allergen sensitivities among some populations, the National Cooperative Inner City Asthma Study's (NCICAS) skin test results of 1,286 children with asthma showed that the most common positive allergen sensitivity was to *Alternaria* (38%) (Eggleston et al., 1999; Kattan et al., 1997). The clearest association between mold exposure and asthma is sensitization to *Alternaria* (generally regarded as an outdoor mold), although this may be because the allergens of this genus (Alt a 1 and Alt a 2) are well characterized relative to other mold species, thus allowing this association to be more easily established (NAS, 2000).

Belanger et al. (2003) found a positive exposure-response between measured levels of mold in the home, as determined by portable air sampling, and wheeze/persistent cough in the first year of life among children whose mothers had asthma, and between mold levels and persistent cough among children of mothers without asthma. Gent et al. (2002) assessed the potential for increased incidence of respiratory symptoms after household exposure (as determined by an airborne sample taken from the living room) to particular fungal genera, namely *Cladosporium* (in 62% of homes) and *Penicillium* (in 41% of homes) in a population of infants at high risk for developing asthma. To the extent that the measured mold sampled represented longer-term exposure concentrations, the study results suggested that the infants studied who were exposed to high levels of *Penicillium* had higher rates of wheeze and persistent cough. The authors also suggested that because there are considerable seasonal variations in some molds, including *Cladosporium*, intermittent exposures may contribute only sporadically to respiratory symptoms. Other molds, such as *Penicillium*, seem to be present at more consistent levels year round. Stark et al. (2003) found a link between exposure to high levels of fungal spores and respiratory ailments – both wheezing and non-wheezing – in infants, though they were unable to determine the mechanisms for such an association. A Russian study associated the presence of mold in homes with numerous respiratory ailments, including bronchitis, asthma, dry cough, and wheezing (Spengler et al., 2004). Previous studies note that relationships between exposure to mold and respiratory symptoms of children are complicated and may depend on a variety of potentially confounding factors, such as the season in which mold samples were obtained (Gent et al. 2002).

Under the appropriate indoor environmental and competitive conditions, molds are also known to produce toxic compounds (mycotoxins), some of which have been observed in laboratory animal studies to have adverse respiratory effects; however, the doses of such toxins required to cause adverse health effects in humans have not been determined (NAS, 2004). In addition, although some human case-studies show an association between inhaled mycotoxins and health effects, these were mostly occupational studies. The most frequently studied mycotoxins are produced by species of *Aspergillus* (e.g., aflatoxins), *Fusarium*, *Penicillium*, *Stachybotrys*, and *Myrothecium* (e.g., satratoxins, trichothecenes) (Burge and Ammann, 1999). Toxins from *Stachybotrys chartarum* have been most commonly associated with lung inflammation and hemorrhage in animal studies (Nikulin et al., 1996, 1997, as cited in Burge and Ammann, 1999) and non-specific symptoms (headaches, sore throats, flu symptoms, diarrhea, fatigue, and dermatitis) in case studies (Dill et al., 1997 and Croft et al., 1986, both as cited in Burge and Ammann, 1999). According to the IOM review of the literature (NAS, 2004), although in vitro and in vivo research on *Stachybotrys chartarum* suggests that effects in humans may be biologically plausible, more extensive research is required to validate this conclusion.

In indoor environments, associations have been reported for pulmonary hemorrhage deaths in infants and the presence of *Stachybotrys chartarum* (Etzel et al., 1998; Flappan et al., 1999; Elidemir et al, 1999; Vesper et al., 2000). Although this specific association has not been conclusive (CDC, 2000), recent research does clearly support the potential for general mycotoxin exposure in the indoor environment to result in adverse effects on respiratory health (NAS, 2000; Sorenson, 1999, Rao et al., 1996; American Academy of Pediatrics, 1998). It has also been suggested that very young children may be especially vulnerable to certain mycotoxins (American Academy of Pediatrics, 1998; Etzel, 2000). For example, Etzel (2000) suggests that exposure to the trichothecene mycotoxins, which are known to be potent protein synthesis inhibitors, may result in pulmonary capillary fragility in the rapidly growing lungs of children younger than one year. However, in several recent review studies (Hardin et al. , 2003; Fung and Hughson, 2003), the reviewers found that although current evidence does support the relationships between excessive moisture, mold growth, and increased prevalence of symptoms due to irritation, allergy, and infection (as well as adverse systemic health effects due to mycotoxin ingestion), current scientific evidence does not establish that human respiratory health has been adversely affected by inhaled mycotoxins in the home, school, or office environment. Kelman et al. (2004) also developed a model of the likelihood of adverse (non-allergic) health effects due to maximum feasible inhaled mycotoxin exposure and found that none of the maximum doses were sufficiently high to cause any adverse effects, which the authors suggest is further evidence that toxic human health effects following inhalation exposure to mycotoxins in mold-contaminated home, school, or office environments is implausible.

Pet Dogs and Cats. The major pet allergens identified and isolated to date include those from the domestic cat (*Felis domesticus*, Fel d 1) and dog (*Canis familiaris*, Can f 1 and Can f 2). The IOM 1999 review found sufficient evidence for the role of cat and dog allergen in asthma exacerbation, but not for either allergen in terms of asthma development. In studies of pet exposure in early life and asthma development, conflicting results have been observed (Chapman and Wood, 2001). In some settings (e.g., where cockroach and dust mite allergen exposure is rare), pet allergens have been shown to be the dominant indoor allergens (Chapman and Wood, 2001). Studies of the characteristics of cat and dog allergens show that they are carried on smaller (<10μm) airborne particulates, and in contrast to dust mite and cockroach allergens, may remain suspended in the air for long periods of time (Chapman and Wood, 2001; NAS, 2000). Due to the adherent nature of cat and dog dander, these allergens may also be transported easily from room to room and deposited in high levels on walls and other surfaces within the home (Chapman and Wood, 2001; NAS, 2000). In addition to the traditional reservoirs in homes, research has also indicated that clothing can be a major source of inhaled cat and dog allergens (O'Meara and Tovey, 2000).

A number of studies also show that the vast majority of homes contain cat and dog allergen even if a pet has never lived there (due to small particle size and ease of transport). For example, in dust samples collected from 831 U.S. homes as part of the National Survey of Lead and Allergens in homes, dog and cat allergens were detected in 100% and 99.9% of homes, respectively, although a dog or cat had lived in only 49.1% of homes in the previous 6 months (Arbes et al., 2004). In the homes without pets, however, pet allergen levels were lower; levels of these allergens in homes are typically highest in homes housing these animals (Chapman and

Wood, 2001; Peterson, et al., 2003). Therefore, occupant choice plays the primary role in determining indoor exposure to pet allergens.

As indicated above, there is ample evidence linking pet allergens to asthma exacerbation and respiratory symptoms; however, this association is not easy to characterize. Gehring et al. (2001) found an association between exposure to levels of cat allergen in excess of 8 μg/g with respiratory symptoms and asthma attacks in adults. Other studies have shown that the relationship between exposure to cat allergen and the risk of sensitization does not follow the same pattern of increasing risk with an increase in exposure that has been reported for dust mite (as indicated by settled dust concentrations). Although moderate exposure to cat allergen (e.g., 8-20 μg/g) has been shown to be associated with sensitization in a significant proportion of the population, the overall risk of sensitization appears to decrease with exposure to higher levels (e.g., > approximately 20 μg Fel d 1/g dust) (Platts-Mills et al., 2001; Sporik et al. 1999). This appears to be a result of a "tolerant" immune response being induced in some children at higher exposure levels (Platts-Mill et al., 2001). An even broader range of protection was suggested by Litonjua et al. (2002), who found that exposure to both dog and cat allergen (at any concentration) in early life was associated with a decreased risk of wheezing in children. The hypothesized protective effect of high-level cat allergen exposure has not been proven, however, and appears to diminish when combined with certain genetic factors, such as maternal history of asthma (Celedon, et al., 2002).

Bacterial Endotoxins. On water damaged materials and in damp areas of homes bacterial growth may also accompany mold growth (NAS, 2004). Endotoxins are biologically active (and in some cases toxic) lipopolysaccharides that are components of some bacterial cell walls. They may be released to the environment when the bacteria die or the cell walls are damaged. In occupational studies of high levels of exposure, endotoxin exposure has been associated with lung disease among workers; the literature on low-level endotoxin exposures reports both adverse and beneficial effects (NAS, 2004). In addition, other agents found in connection with bacterial endotoxins, including β(1→3)-glucans, may have a role in health outcomes attributed to endotoxin exposure (NAS, 2004).

The relationship between bacterial endotoxin exposure and asthma symptoms is particularly difficult to characterize. Some studies have associated endotoxin with asthma exacerbation, while others have noted that endotoxin exposure may have a protective effect. This protective effect is related to the “hygiene hypothesis” discussed later in this paper.

Michel et al. (1996) found that the presence of endotoxin in house dust was significantly related to the severity of asthma symptoms in individuals sensitized to the dust mite. On the other hand, a study of children in rural Germany, Austria, and Switzerland produced quite different results. In children from farming households, who are routinely exposed to high levels of environmental endotoxin, the authors observed a significantly decreased risk of hay fever, sensitization, atopic wheeze, and atopic asthma. This effect was seen in children from both farming and nonfarming households, indicating that even low levels of exposure to endotoxin may protect against atopic diseases. (Braun-Fahrlander, 2003). Gehring et al. (2002) found similar results in a study of 740 atopic and non-atopic children in Germany. Data from this study suggested that exposure to endotoxin in house dust was negatively associated with allergic sensitization in children; this

protective effect grew stronger with higher endotoxin levels (Gehring et al., 2002). A longitudinal analysis of wheezing in children found that, while exposure to house dust endotoxin increased the risk of wheezing in early life, the risk diminished rapidly as the children aged, with endotoxin exposure possibly protecting against wheezing later in childhood (Litonjua et al., 2002). In a review of existing literature on the subject, Eder and von Mutius (2004) urged caution among those who claim that exposure to bacterial endotoxin protects against asthma, pointing out that this protective effect was not observed in cases of non-atopic asthma and suggesting that future studies investigate whether endotoxin itself provides protection or whether it acts as an indicator for some other environmental variable.

Housing characteristics associated in the literature with endotoxin levels in homes, although not consistently, include presence of pets in the home, contact with farm animals, number of people living in the house, cleaning habits (frequency and methods), moisture levels, room locations, and insulation. The predominant factor identified in the majority of the literature, however, appears to be current or past ownership of indoor dogs. Park et al. (2001) found that airborne endotoxin levels in Boston-area dwellings were most strongly affected by presence of dogs, moisture sources (lack of dehumidifier), and increased amounts of settled dust, although this multivariate model explained only 42% of the variability of airborne endotoxin levels observed. Wickens et al. (2003) also found that (in 77 New Zealand homes) endotoxin levels were positively associated with dogs inside, as well as number of household occupants, reusing vacuum dust collection bags, steam cleaning or shampooing the carpet, and high relative humidity. Lower endotoxin was associated in this study with floor insulation and north-facing living rooms. In a study of the homes of 86 infants with wheeze in metropolitan Denver, Colorado, Gereda et al. (2001) found house dust endotoxin levels to be associated with only two home characteristics – animals in the home and the presence of central air conditioning. Although levels were most strongly associated with animals, central air conditioning was associated with lower house dust endotoxin levels particularly during the summer months of use. No significant associations were observed between endotoxin levels and home dampness or cleaning frequency. In another study, Gehring et al. (2004) also found endotoxin levels in mattress dust (of 2157 infants and 2108 mothers) to be associated with a number of factors typically discussed in the framework of the hygiene hypothesis, including pet-ownership, contact with pets, and number of persons living in the home; however, none of these factors and not even a combination of factors explained the variability of endotoxin levels between homes in this study.

In response to previous research that had observed lower frequencies of asthma and hay fever in children with contact to livestock, Waser et al. (2004) investigated potential linkages between home and lifestyle characteristics of farm and non-farm families, the amount of endotoxin in homes, and the occurrence of asthma. Analysis of endotoxin levels in dust samples from the living room floor and child's mattress of 319 farmers' families and 493 non-farming families showed an association between the child's activity on the farm and indoor home endotoxin levels (higher endotoxin levels were associated with higher levels of farm activity), thus indicating that proximity to rural areas may be an important factor.

Viruses. The IOM 1999 review found evidence of an association between certain types of viruses and asthma development and exacerbation. In the case of respiratory syncytial virus (RSV), there is limited or suggested evidence of an association between the virus and both

asthma development and exacerbation, while sufficient evidence exists of an association between rhinovirus (RV) and asthma exacerbation only (NAS, 2000). Research to date indicates that viruses are a major trigger for acute asthma attacks in children, though the mechanisms by which viruses influence wheezing are poorly understood at this time (Gern, 2004). In one study the effect of viral infection on asthma exacerbation was significantly affected by exposure to high levels of NO_2 during the week immediately preceding the infection. Children who were exposed to elevated levels of personal NO_2 experienced more severe asthma symptoms and reduced lung function during virus-triggered asthma exacerbations; this trend remained for all types of viruses together and for both RSV and RV individually (Chauhan et al., 2003).

In contrast, in a study of 1,314 children born in five German cities and followed from birth to the age of 7 years, Illi et al. (2001) found that repeated viral infections (other than lower respiratory tract infections) early in life may reduce the risk of developing asthma up to school age, a finding that is consistent with the hygiene hypothesis. Repeated lower respiratory tract infections in the first three years of life, however, showed a positive association with wheeze up to the age of seven years.

Calvani et al. (2004) investigated possible effects of infection-related maternal stress during pregnancy and later development of atopic and nonatopic asthma in children. Results of the case-controlled study enrolling 338 children with asthma and 467 controls showed that flu and fever episodes during pregnancy (mainly the third trimester) were significantly associated with asthma in children, suggesting that prenatal infective complications may contribute to the development of asthma in children.

Another viral respiratory disease that can potentially affect children, hantavirus pulmonary syndrome (HPS), is a rodent-related exposure that in some cases may be associated with housing and neighborhood conditions. HPS is discussed in Section 3.3.5 of this paper on injury. Housing factors related to rodent exposure in homes, such as condition of home (e.g., holes in walls), access to food and water sources in the home, and home sanitation, were also discussed previously (Sections 3.4.3, 3.4.5).

The Hygiene Hypothesis. As can be seen from the literature related to bacterial endotoxins and viral infections, additional research is needed to better characterize the relationships between infections and asthma, as well as to determine housing or neighborhood conditions that may be related to these exposures. A related concept, known as the "hygiene hypothesis," has spawned a number of recent studies. The hygiene hypothesis suggests that children's immune systems are not being developed normally at a young age due to a general lack of exposure to infectious agents (Ball, 2000; Arruda et al., 2001). Research in the U.S. and Europe has found evidence that exposure to microbial organisms via lifestyle characteristics such as day care attendance, having multiple siblings, close proximity to farming practices, and observation of anthroposophic principles (a philosophy embracing natural lifestyles, including organic crop cultivation, homeopathic medicine, and restriction of vaccinations), may decrease the risk of atopy and asthma (Liu and Szefler, 2003; von Mutius, 2002; Braun-Fahrlander et al., 2002). The inverse relationship between atopy-related illnesses and microbial exposure observed in the studies above is by no means universal, however. Celedon et al. (2003) found that the protective effect of day care attendance was only observed in children without maternal history of asthma.

Other research casts doubt over the hygiene hypothesis in its entirety. Results of the International Study of Asthma and Allergies in Childhood showed that there was not a lower prevalence of asthma in some underdeveloped countries (i.e., countries with poor hygiene and high infection rates) compared with those in the developing world (ISAAC Steering Committee, 1998; Arruda et al., 2001). It is possible, however, that children in developing countries are exposed to different sensitizing agents, thereby changing their risk level and subsequent expression of disease. After extensive review of studies investigating the relationship between the number of siblings in a family and allergic disorders, Karmaus and Botezan (2002) concluded that the hygiene hypothesis failed to explain inconsistent study results.

3.4.6 Neighborhood Attributes and Other External Factors Related to Asthma/Respiratory Outcomes

While virtually any indoor environment could contain allergenic substances or irritants, the literature shows that numerous factors external to housing may have an impact on allergen concentrations and the particular substances to which children might become sensitized. These factors include location, proximity to traffic, ambient air pollution, and neighborhood or household safety. The following paragraphs discuss each factor individually.

Location. The location of a home can play a major role in the types and concentrations of substances measured in indoor air. Some researchers have found marked differences in the types of asthma triggers found in homes in inner-city areas compared to suburban or rural areas (Kitch, 2000; Kattan et al., 1997). In general, Crain et al. (2002) found that inner-city children were more likely to be sensitized to multiple indoor allergens and to live in surroundings associated with allergen exposure. A Baltimore study found indoor concentrations of many airborne pollutants to be higher in urban residences than in suburban homes (Simons et al., 2004). It has also been suggested that the elevated levels of pet allergens (which are very easily transported on clothing, etc.) observed in many homes without pets, particularly among demographic groups in which pet ownership is more prevalent, may be a result of the community serving as an important local source of these pet allergens (Arbes et al., 2004).

Increased allergen levels are not the only factor differentiating urban from suburban environments, however. Asthmatics living in low income, urban housing have been found to have patterns of specific sensitivities that differ from other populations, with a higher frequency of sensitivity to cockroaches, mice, and molds and less frequent sensitivity to cats, dogs, and house dust mites (Eggleston, 2000; Eggleston et al., 1999; Phipatanakul, 2000a and 2000b). Cockroaches are of particular concern, with some suggesting that these insects may be the sole sensitizing agent for many children living in inner-city areas (Alp, 2001). Kilpelainen et al. (2000) found that living on a farm has a protective effect against allergic rhinitis, and also (but more weakly) against asthma and wheezing irrespective of family size. In line with the hygiene hypothesis, the authors suggest that environmental exposure to immune modulating agents, such as environmental mycobacteria and actinomycetes, may possibly explain the finding.

Ambient Air Pollution. A key factor potentially impacting indoor pollutant concentrations and respiratory health is proximity to sources of ambient air pollution. In industrialized areas, residents may be exposed to industrial emissions on a routine basis. A Korean study compared the prevalence of asthma, bronchial hyper-responsiveness, and atopy of children living in a

heavily industrialized area with those living in a less polluted neighborhood. Results indicated that both asthma and bronchial hyper-responsiveness were significantly associated with living in a polluted environment, though atopy was not (Kim et al., 2001). Similar results were found in a retrospective U.S. study that utilized hospital and emergency room records along with other data sources to investigate the relationship between proximity to pollution and respiratory disease. This study found strong positive associations between proximity to pollution sources and health care utilization, along with clusters of asthma cases surrounding high-traffic areas and suspected emissions sources (Oyana and Lewbuga-Mukasa, 2004).

Traffic. Living in areas with high vehicle traffic has been associated with respiratory illness (Nicolai et al., 2003; Spengler et al., 2004) and with exacerbation of symptoms in children and adults who already have respiratory ailments such as asthma (Van der Zee et al., 1999; Gavett and Koren, 2001). An Italian study linked residence in areas with heavy vehicular traffic with an increased risk of respiratory infection in early childhood and wheezing at school age (Ciccone et al., 1998). These effects may be attributable to the pollutants associated with vehicle exhaust, such as particulate matter and gaseous compounds. While such results seem to suggest that traffic-related pollution may contribute to asthma development, this association has not been proven. A study in San Diego County, California, found no evidence to associate high traffic counts in the surrounding community with increased asthma prevalence among children; however, the number of medical visits among asthmatic children increased with traffic levels, suggesting once again that exhaust pollutants may contribute to asthma exacerbation (English et al., 1999).

The external factors discussed thus far have been either measurable (e.g., ambient air pollution) or clearly evident (e.g., residence in an urban environment); however, less tangible factors may also play a role in respiratory health. The Inner-City Asthma Study (ICAS) investigated the relationship between exposure to violence and asthma symptoms among urban children. Results showed that inner-city children were at great risk for exposure to violence and that increased exposure was associated with asthma morbidity, even after adjusting for socioeconomic indicators. However, ICAS researchers acknowledged that other factors, such as psychological stress and caretaker behaviors (e.g., smoking or failing to administer asthma medications), attenuated the association between violence and asthma (Wright et al., 2004).

3.4.7 Behavioral and Socioeconomic Factors Related to Asthma/Respiratory Outcomes and Interaction with Obesity

While much of the research on asthma to date has focused on biological and other specific risk factors, some studies have attempted to identify the role of behavioral and socioeconomic factors in asthma development and exacerbation. Behavioral risk factors include choices such as owning a pet or smoking. As discussed in Section 3.4.5, pet dander has allergenic properties, and the presence of a cat indoors has been established as a risk factor for asthma exacerbation. As for smoking, the IOM 1999 review (NAS, 2000) found sufficient evidence of a causal relationship between ETS exposure and asthma exacerbation. ETS exposure was also found to be associated with asthma development in preschool aged children, and limited evidence of an association was observed between ETS exposure and asthma exacerbation in adults and older children (NAS, 2000). DiFranza et al. (2004) suggested that ETS is the most harmful and ubiquitous of environmental exposures to children, citing associations between ETS exposure

and reduced lung growth, childhood asthma, and respiratory tract infections, among other non-respiratory illnesses.

Several recent studies have uncovered an apparent relationship between socioeconomic status (SES) and asthma. Residence in low-income, urban areas has been implicated as an important risk factor for all children (Aligne et al., 2000; Krieger et al., 2000; Brugge et al., 2003; Litonjua et al., 1999). Eggleston (2000) reported disproportionately high rates of increased asthma incidence among children and African-Americans in the United States. Research has suggested that a large portion of the observed racial and ethnic differences in asthma prevalence is explained by factors related to income and education (Litonjua et al., 1999). Sarpong et al. (1996) attempted to further isolate specific risk factors by evaluating the contribution of race, SES, and place of residence to the prevalence of cockroach allergen exposure and sensitization in asthmatic children. Their results identified race and SES as independent and significant predictors of sensitization to cockroach allergens, regardless of whether the residence was located in an urban or suburban environment. Further complicating the matter, a complete explanation for the commonly observed SES-health gradient does not currently exist. Some researchers hypothesize that a majority of the variability can be explained by a model that includes differential (and cumulative) exposure to environmental risk, including individual environmental conditions such as hazardous wastes and other toxins, ambient and indoor air pollution, water quality, crowding, and ambient noise, as well as the physical quality of specific settings such as the home, school, work environment, and neighborhood (Evans and Kantrowitz, 2002).

Finally, asthma may also be influenced by interaction with other health outcomes, which may also themselves be related to housing or neighborhood factors. For example, one interaction that has been studied is the observed linkage between asthma and obesity. Castro-Rodriguez et al. (2001) investigated the possibility of a causal relationship between obesity and asthma, as suggested by recent concomitant increases in the prevalence of both, in a cohort of children assessed at ages of approximately 6 (n = 688) and 11 (n = 600) years old. Study results indicated that females (but not males) who become overweight or obese between these two ages have an increased risk of developing new asthma symptoms and increased bronchial responsiveness during the early adolescent period. Similarly, in a longitudinal study of 3,792 participants in the Children's Health Study (Southern California) who were asthma-free at enrollment, Gilliland et al. (2003) found that the risk of new-onset asthma over the course of the study was higher among children who were overweight.

3.4.8 References for Section 3.4

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3.5 LITERATURE ON THE RELATIONSHIPS BETWEEN HOUSING AND NEIGHBORHOOD CHARACTERISTICS AND OBESITY AND DEVELOPMENT

3.5.1 Additional Information on the Literature Review Approach for Obesity/Physical Development

Hypothesis 5 of the National Children's Study addresses obesity and altered physical development (see Appendix A). Hypothesis 5.5 is specifically related to housing and neighborhood characteristics as it tests whether environmental factors such as distance to parks, availability of walking routes in the neighborhood, and neighborhood safety are associated with risk of obesity and insulin resistance. Also related to housing and neighborhood characteristics, Hypothesis 5.7 tests whether *in utero* and subsequent exposure to environmental agents that affect the endocrine system (bisphenol A, atrazine, and lead) results in altered age at puberty. As many of the chemicals that may act as endocrine disruptors are also neurodevelopmental/neurotoxic, much of the information related exposures to these chemicals (e.g., pesticides, PCBs) in residential settings was also covered in other sections of this report, including Section 3.1.3 on maternal exposures/adverse pregnancy outcomes and Section 3.2.4 on neurodevelopmental outcomes. Only literature specific to chemical exposures and altered puberty and development were a focus in the section.

3.5.2 Overview

Obesity. Obesity is a growing epidemic in the United States. In 2004, approximately 66% of Americans are overweight, and 33% are considered obese (Wakefield, 2004). Obesity is increasing not only among adults but among young people, as well. In the last 20 years, the number of overweight and obese children in the U.S. has more than doubled. About 15% of children aged 6-18 are now obese; this figure jumps to 26% for Hispanic and black children (Schmidt, 2003). At the same time, data on childhood activity levels suggest that children in general are becoming more sedentary. The Centers for Disease Control and Prevention reported a 6% decline in the percentage of children attending daily physical education classes between 1995 and 2001. Furthermore, children spend less time walking and more time riding in automobiles (Schmidt, 2003).

The prevalence of obesity in children carries with it a number of related health problems. The incidence of type 2 diabetes among U.S. children has grown more than 10-fold since the early 1980s (Schmidt, 2003). Two recent studies linked being overweight in childhood with an increased risk of developing asthma (Gilliland et al., 2003; Castro-Rodriguez et al., 2001). Sleep apnea, stroke, hypertension, cardiovascular disease, and depression are also associated with being overweight; and childhood obesity elevates the risk that a child will develop potentially fatal health problems in adulthood (Schmidt, 2003). Experts have estimated that up to 300,000 people die prematurely in the U.S. each year from conditions related to obesity (Wakefield, 2004; Brownson et al., 2004).

Perhaps the most recently publicized link between the occurrence of overweight and obesity in the United States is with the physical or "built" environment. For example, a survey conducted by Jackson and Kochtitzky (2001) suggests that a person's immediate environment (neighborhood) is one of the more important determinants of physical activity. The built environment influences weight management by affecting both food intake and energy expenditure. Some researchers contend that the pervasiveness of fast food and low-energy leisure activities have a tremendous impact on childhood weight gain; children in the U.S. spend more time watching television and playing video games than participating in any other form of recreation (Fitzgibbon and Stolley, 2004). Environmental conditions may also affect an individual's desire or ability to exercise (Brownson et al., 2001). For example, neighborhood design may impact the willingness of residents to walk or participate in other outdoor physical activities in the area (Saelens et al., 2003; Giles-Corti et al., 2003). Negative perceptions of a particular area, even if unfounded, may prevent parents from allowing their children to walk or ride bicycles in the neighborhood, limiting opportunities for the children to be physically active (Timperio et al., 2004).

However, as evidenced by the limited amount of data available on the subject, researchers are still in the early stages of understanding the connections between obesity trends and the environment. Differences of opinion exist in the scientific community on what constitutes a healthy diet, and scientists cannot conclusively state that altering neighborhood infrastructure will necessarily lead to increases in physical activity among children or adults (Wakefield, 2004). Furthermore, many of the studies on neighborhood characteristics, exercise, and obesity focus primarily on adults, and it is difficult to extrapolate these results to child populations (Schmidt, 2003). While additional research efforts are needed to fully understand the determinants of obesity among children in the U.S., it is clear that a number of environmental and policy factors related to the built environment are associated with physical activity and should be considered as potentially important factors in childhood obesity (Brownson et al., 2001).

Physical Development and Altered Age at Puberty. Of increasing concern in recent years is the potential for certain hormone-mimicking chemicals in the environment to disrupt components of the human endocrine system, potentially interfering with function of the brain, pituitary, reproductive, thyroid, and other components of the endocrine system. However, although a variety of endocrine disrupting chemicals have been researched extensively in laboratory animal studies and adverse health and developmental effects observed in wildlife populations, information on the human effects of endocrine disruptors is limited; as a result, the extent of harm caused by exposure to these compounds at background levels common in the environment is debated (NRC, 1999). For example, with apparent trends towards a decreasing age at menarche in the U.S. (Kaplowitz et al., 2001; Midyett et al., 2003), some have pointed to endocrine disruptors as a possible cause (Blanck et al., 2000), although others have found no linkages (Warner et al., 2004). Based on available suggestive evidence and the need for additional information, the U.S. Environmental Protection Agency initiated the Endocrine Disruptor Screening Program in 1996 to test chemicals and environmental contaminants for their potential to affect the endocrine systems of humans and wildlife.

An overview of the available research identified in the course of this literature search on housing and neighborhood characteristics linked to either children's exposure to endocrine disruptors or risk factors for obesity is presented in Table 3.5-1 below.

Table 3.5-1. Summary of Key Literature on Housing and Neighborhood Characteristics Associated with Obesity or Altered Physical Development

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
GENERAL STUDIES AND REVIEWS		
General Housing	Limited data available on the relationship between built environment and childhood obesity	Schmidt 2003
General Neighborhood	Immediate environment (neighborhood) is one of the more important determinants of physical activity	Jackson and Kochtitzky 2001
HYPOTHESIZED STRUCTURAL/PHYSICAL RISK FACTORS		
Housing type and age		
Structure, construction, condition		
Electrical system		
Fire Related Factors		
Building Materials		
HVAC		
Moisture		
Cleanliness		
Safety devices		
HYPOTHESIZED CHEMICAL RISK FACTORS		
General endocrine disruptors	Review study: Although laboratory and wildlife studies provided compelling evidence for an association between exposure to endocrine disruptors and structural and functional abnormalities in animals, additional research is needed regarding human health effects	NRC 1999
Pesticides	Exposure to endocrine disruptors in the residential environment can occur from a variety of sources, including commercial pesticide products	NRC 1999
Other organic chemicals	Media sampling in 120 homes showed that many suspected endocrine disruptors were found in homes as a result of use of consumer products in the homes (52 found in air and 66 found in dust)	Rudel et al. 2003
	Exposure to endocrine disruptors in the residential environment can occur from a variety of sources, including certain commercial products containing synthetic organic chemical (e.g., cleaners, materials containing flame retardants)	NRC 1999
	Children of about 2,000 Taiwanese people accidentally exposed to high levels of PCBs from contaminated cooking oil in 1979 (i.e., the Yu-cheng cohort) showed developmental health effects including reduced intelligence/delayed development, retarded growth, physical abnormalities, and sperm abnormalities in young boys and men after puberty.	Guo et al. 2004
	Women in the Yu-cheng cohort who were exposed to high levels of PCBs showed menstrual abnormalities, also suggesting potential reproductive effects from the PCB exposure.	Yu et al. 2000
	In a study of accidental food chain exposures of more than 4,000 people in Michigan to polybrominated biphenyls (PBBs) in 1973, girls (327) exposed to high levels of PBB in utero, and in many cases through breast feeding, had an earlier age at menarche than girls exposed to lower levels of PBB in utero.	Blanck et al. 2000
	No association was found between blood levels of dioxin (another suspected endocrine disruptor) and age at menarche in 282 women exposed to very high-levels of dioxin as children (postnatal but pre-puberty) as a result of a chemical explosion in Seveso, Italy.	Warner et al. 2004
Combustion by-products		

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Lead	In an analysis of NHANES data, environmental exposures to lead (at levels as low as 3 µg/dL) delayed growth and pubertal development in African-American and Mexican-American girls.	Selevan et al. (2003)
	In an analysis of NHANES data, higher blood lead levels were significantly associated with delayed attainment of menarche and pubic hair among U.S. girls, but not with breast development.	Wu et al. 2003
Asbestos, fiberglass		
Other inorganic chemicals		
Also see "Ambient air pollution" and "Traffic" rows under External Factors Affecting Housing		
HYPOTHESIZED BIOLOGICAL RISK FACTORS		
Multiple allergens		
Dust mites		
Cockroaches		
Other insects (ticks, fleas, mosquitoes)		
Mice		
Rats		
Other rodents		
Molds		
Pets		
Bacteria, endotoxins, microbial VOCs		
Other triggers (e.g., viral agents, parasites)		
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS		
Location	Sprawl is associated with both increased time spent in cars and increases in body weight	Frank et al. 2004
	New location patterns produced by suburban sprawl are an important cause of rising obesity rates	Vandegrift and Yoked 2004
	The design of most new residential areas reflects the supposition that people will travel by car to most destinations	Jackson and Kochtitzky 2001
	Altering neighborhood infrastructure will not necessarily lead to increases in physical activity among children or adults	Wakefield 2004
	A "fitness crisis" exists among children in urban areas of the U.S., as determined by comparing exercise endurance times of inner-city U.S. children to a reference population in a smaller Canadian town	Chatrath et al. 2002
	Obesity is more prevalent among rural than urban adults	Patterson et al. 2004
Zoning/building codes	Mixed land use is the most important variable of the built environment related to obesity; As walking distance and mixed land-use within a neighborhood increase, the likelihood of obesity decreases	Frank et al. 2004
	States increasing the amount of developed land (holding population constant) showed larger increases in obesity	Vandegrift and Yoked 2004
	The perception of no shopping areas within walking distance is related to obesity	Giles-Corti et al. 2003
	A significant association exists between the percentage of people who walk to work and environmental score, a ranking based on neighborhood characteristics such as the availability of walking routes, degree of traffic threats, mix of facilities in the area, and visual aesthetics	Craig et al. 2002
Ambient air pollution		
Traffic		See Brownson et al. 2001 below
	The perception of threats from area traffic contribute significantly to a neighborhood's environmental score	Craig et al. 2002

HOUSING & NEIGHBORHOOD RISK FACTORS	KEY FINDINGS	CITATION
Noise		
Crime rates, violence, neighborhood safety	The greatest perceived barrier to physical activity is lack of safe place to exercise	Jackson and Kochtitzky 2001
	A positive relationship exists between safe access to recreational facilities and physical activity	Fitzgibbon and Stolley 2004
	Perceptions of safety, good lighting, and availability of sidewalks are linked to physical activity	Schmidt 2003
Recreational facilities, playground equipment	Children's activity correlates highly with time spent outdoors and access to recreational areas	Schmidt 2003
	Inadequate access to recreational areas is associated with obesity	Giles-Corti et al. 2003
Pedestrian and bicycle access	Children's and parents' perceptions of the local neighborhood may influence children's likelihood of walking or cycling	Timperio et al. 2004
	Urban sprawl is associated with decreased rates of walking and biking and with increased rates of automobile travel	Frumkin 2002
	Sprawl is associated with decreased time spent walking and increased rates of obesity and hypertension	Ewing et al. 2003
	A more walkable neighborhood (as reported by higher residential density, land use mix, street connectivity, aesthetics, and safety) is associated with higher physical activity and lower obesity prevalence in adults	Saelens et al. 2003
	Activity levels increase with overall walkability (as measured by residential density, street connectivity, and mixed uses)	Schmidt 2003
	Students are four times more likely to walk to schools built before 1983 than to those built more recently	Jackson and Kochtitzky 2001
	Perceptions of safety, good lighting, and availability of sidewalks are linked to physical activity	Schmidt 2003
	Neighborhood characteristics, including the presence of sidewalks, enjoyable scenery, heavy traffic, and hills, are positively associated with physical activity in adults	Brownson et al. 2001
	Poor pedestrian access is related to overweight	Giles-Corti et al. 2003
		See Craig et al. 2002 above
Water hazards		
HYPOTHESIZED BEHAVIORAL & SES RISK FACTORS		
SES mediators	Race, education, and income are strongly correlated with perceived neighborhood environmental factors and access to places for physical activity	Huston et al. 2003
	Latino children are associated with reduced physical activity levels at home when compared to white children	Fitzgibbon and Stolley 2004
	Less educated individuals and those with lower socioeconomic status are less likely to exercise than more educated people of higher socioeconomic status	King et al. 1992, as cited in Fitzgibbon and Stolley 2004
Other behavioral factors	Reported personal barriers to physical activity include lack of time, feeling too tired, obtaining enough exercise at one's job, and no motivation to exercise	Brownson et al. 2001

As can be seen from Table 3.5-1, a substantial body of research exists on the relationships between obesity and neighborhood physical and social characteristics. Other risk factors for obesity that were identified in this literature search relate to behavioral/socioeconomic factors. Limited literature was also identified that examined exposures (possibly residential in some cases) to endocrine disruptors and altered physical development or age at puberty.

3.5.3 Chemical Attributes of Housing/Neighborhoods Affecting Physical Development

In 1999, the National Research Council (NRC) conducted an independent review of available information on potential human health effects resulting from exposure to endocrine disruptors (or "hormonally active agents") in the environment, and concluded that although laboratory and wildlife studies provided compelling evidence for an association between exposure to hormonally active agents and structural and functional abnormalities in animals, additional research was needed regarding human health effects (NRC, 1999). Hypothesized human health effects of hormonally active chemicals investigated in various studies reviewed by the NRC (1999) and another review study by Landrigan et al. (2004) include altered sexual development, decreased fertility, reproductive organ birth defects, altered sex ratios, neurodevelopmental impairment, thyroid disruption, diabetes, immunological effects, and cancer. The reviewers noted that these hypothesized health effects were largely based on animal studies, but also included some human epidemiological data from accidental exposure scenarios (e.g., PCBs in Taiwan and dioxins in Italy) and background exposure studies (e.g., Dutch cohort studies). Wildlife studies in the NRC and Landrigan literature reviews cited reproductive disorders in wildlife, such as morphologic abnormalities, eggshell thinning, population declines, impaired viability of offspring, altered hormone concentrations, and changes in social/sexual behavior.

Environmental chemicals cited in the literature that may act as endocrine disruptors include a variety of substances, such as:

- Pesticides [insecticides such as dichlorodiphenyltrichloroethane (DDT), endrin, aldrin, dieldrin, lindane, chlordane, toxaphene, endosulfan, methoxychlor, kepone, dicofol, chlordane; herbicides such as alachlor, atrazine and nitrofen; fungicides such as benomyl, mancozeb and tributyl tin; nematocides such as aldicarb]
- Pharmaceuticals [drug estrogens]
- Chemicals associated with consumer goods/household products [chemicals associated with plastics (bisphenol A, phthalates), breakdowns products of detergents and associated surfactants (including nonylphenol and octylphenol), polybrominated diphenyl ethers (PBDEs), perfluorooctane sulfonate (PFOS)]
- Industrial chemicals [polychlorinated biphenyls (PCBs), dioxin and benzo(a)pyrene, hexachlorobenzene, polycyclic aromatic hydrocarbons (PAHs)]
- Heavy metals [arsenic, lead, mercury, and cadmium]
- Natural hormones such as the phytoestrogens

[NRC, 1999; Landrigan et al, 2004; Brouwer et al., 1999; Rogan and Ragan, 2003; Legler and Brouwer, 2003; Wu et al., 2003; www.ourstolenfuture.com/Basics/chemlist.htm]

Exposure to hormonally active agents (HAAs) in the residential environment can occur from a variety of sources, such as via contaminated drinking water, polluted air, ingesting food, and contacting or ingesting contaminated soil or dust, as well as through the use of certain commercial products containing synthetic HAAs (e.g., cleaners, pesticides, cosmetics and food additives) (NRC, 1999). Rudel et al. (2003) investigated potential indoor exposures to numerous endocrine disruptors found in consumer uses. Results of analyses of indoor air and dust from 120 homes for 89 organic chemicals identified as potential endocrine disruptors showed that fifty-two of the compounds were present in air, with the most abundant compounds

in air including phthalates (plasticizers, emulsifiers), o-phenylphenol (disinfectant), 4-nonylphenol (detergent metabolite), and 4-tert-butylphenol (adhesive). Sixty-six endocrine disrupting compounds were present in dust samples taken from homes, with frequent detections of penta- and tetrabrominated diphenyl ethers (flame retardants) and numerous pesticides in dust. An intermediate of a flame retardant banned in 1977 (2,3-dibromo-1-propanol), as well as the banned pesticides heptachlor, chlordane, methoxychlor, and DDT, were also frequently detected in dust and air, suggesting limited indoor degradation over time (Rudel et al., 2003). According to the authors, for 15 compounds detected concentrations exceeded government health-based guidelines, but no guidelines are available for 28 compounds, and existing guidelines do not consider endocrine effects.

An overview of selected hormonally active agents and their possible sources is in Table 3.5-2 below.

Table 3.5-2. Possible Endocrine Disruptors Common in the Environment and their Uses or Sources

Pesticides	
DDT	Persistent organochlorine insecticide; banned in the U.S. but still used in developing countries; ubiquitous in environment from past use and associated with numerous adverse reproductive effects in wildlife
Chlordane	Persistent organochlorine insecticide; banned in US., but widely used in past residentially on home foundations for termite control
Malathion	Organophosphate insecticide; currently used on agricultural food/feed crops and livestock; lawns, gardens, ornamental trees, shrubs, and plants in residential settings; also mosquito control and Boll Weevil Eradication Program, and pets for pest control.
Industrial Chemicals	
PCBs	Persistent organochlorine; banned in US since 1997; ubiquitous in environment and may be found in older products (electrical/ hydraulic equipment, consumer products, e.g., fluorescent light fixtures, small capacitors in appliances like microwaves, ink, caulking compounds, carbonless copy paper, plastics and plasticizers, paints, adhesives, flame retardants, and pesticide carriers)
Dioxins/Furans	Unintentional by-products of combustion (industrial and non-industrial, e.g., trash burning) and various industrial process; ubiquitous in environment, primary exposure via food (consumption of animal fats)
Industrial/Consumer Products	
Bisphenol A	Chemical intermediate for numerous industrial products (e.g., plastics, polymers, resins, dyes and flame retardants); also used in dental sealants
Phthalates	Used as plasticizer in polyvinyl chloride, and many consumer products, such as paper coatings, adhesives (rubber cement), solvents, acaricides, cosmetic components, fixatives in perfumes, and erasable and printing inks
PFOS	Key ingredient in 3M Scotchgard; widely used for past 40 years in a variety of industrial and consumer products (e.g., upholstery, apparel, plastics, electronics, fire extinguishing foams) to impart fire resistance and oil, stain, grease, and water repellency.
PBDE, PBB	PBDE is a persistent organochlorine used commercially in US (banned in Europe) as flame retardant in foams and resins; consumer products include television sets, computers, computer monitors and printers, carpets, furniture and upholstery. PBB is a closely related chemical used for similar purposes, but banned in 1976

The literature on potential endocrine disruptors includes studies of both low-level background exposures and acute high-level exposure incidents. For example, health effects of PCBs have been investigated in numerous laboratory animal studies, including several that demonstrated endocrine effects (as well as other neurocognitive effects) at PCB tissues concentrations similar to the human body burden levels found in the general population in industrialized countries at background exposure levels (Brouwer et al., 1999). The potential for PCBs to act as endocrine disrupters in human populations at background exposures was reviewed by Brouwer et al. (1999), who found several studies in the literature involving human infants. The reviewers reported that the literature supported subtle changes in thyroid hormone levels and neurobehavioral parameters with prenatal exposure to PCBs, although some studies were limited (e.g., the effects were primarily, but not exclusively, attributed to PCBs) and some inconsistencies were present in the neurobehavioral and thyroid hormone findings, emphasizing the need for further investigations.

In addition, a few human populations that have been accidentally exposed to high levels of hormonally active agents have been followed longitudinally for potential health effects. For example, serial studies have been conducted on children of about 2,000 Taiwanese people accidentally exposed to PCB-contaminated cooking oil in 1979 (i.e., the Yu-cheng cohort). Observed health effects of high-level prenatal PCB exposure in this population include reduced intelligence/delayed development, retarded growth, physical abnormalities, and sperm abnormalities in young boys and men after puberty (Guo et al. 2004). Women in this cohort who were exposed showed menstrual abnormalities, also suggesting potential reproductive effects from the PCB exposure (Yu et al., 2000). In a study of accidental food chain exposures of more than 4,000 people in Michigan to polybrominated biphenyls (PBBs) in 1973, Blanck et al. (2000) assessed pubertal development in 327 females 5-24 years of age who were exposed to PBB *in utero* and, in many cases, through breastfeeding. Girls exposed to high levels of PBB *in utero* had an earlier age at menarche than girls exposed to lower levels of PBB in utero. In contrast, Warner et al. (2004) found no association between blood levels of another suspected endocrine disruptor, dioxin, and age at menarche in 282 women exposed to very high-levels of dioxin as children (postnatal but pre-puberty) as a result of a chemical explosion in Seveso, Italy. The authors note that, consistent with animal studies, dioxin exposures *in utero* may be more important than those postnatally with regard to altered age at puberty.

In two separate studies of blood lead data from the Third National Health and Nutrition Examination Survey (NHANES), analyses were conducted to investigate whether background level exposures to lead are linked to altered growth, puberty, or other endocrine function (Selevan et al., 2003; Wu et al., 2003). Selevan et al. (2003) looked at the relation between blood lead concentration and pubertal development in 600 non-Hispanic white, 805 non-Hispanic African-American, and 781 Mexican-American girls (defined as 8 to 18 years of age). Data analyses suggested that environmental exposures to lead (at levels as low as 3 μg/dL) delay growth and pubertal development in girls, although only the African-American and Mexican-American girls showed significant delays. In a similar analysis, Wu et al. (2003) compared blood lead concentrations with measures of puberty in a sub-population of 1,706 NHANES girls (defined as 8-16 years of age), and also found (after adjustment for race/ethnicity, age, family size, residence in metropolitan area, poverty income ratio, and body mass index) that higher

blood lead levels were significantly associated with delayed attainment of menarche and pubic hair among U.S. girls, but not with breast development.

3.5.4 Neighborhood and Other External Factors Affecting Obesity and Physical Development

Numerous external factors, primarily at a neighborhood level, have been cited as potential contributors to the rise in overweight and obesity among U.S. children. The general location of a residence, community design, urban sprawl, traffic, safety, and the availability of recreational opportunities have all been studied in relation to obesity rates. Location includes characteristics such as proximity to industrial or agricultural areas, as well as community type (e.g., urban, suburban or rural). Each of these factors is discussed in subsequent paragraphs.

Community Design and Urban Sprawl. Of the characteristics related to community design, urban sprawl has received perhaps the most attention with regard to its effects on the environment and public health. Sprawl has been defined as increases in the amount of developed land, holding population constant (Vandegrift and Yoked, 2004). Using state-level obesity data from the 1990s, Vandegrift and Yoked (2004) found that states increasing the amount of developed land (holding population constant) showed larger increases in obesity. Frank et al. (2004) have also found a relationship between measures of sprawl and body mass.

Urban sprawl is considered to be the outcome of four related factors: low population density; an inadequate mix of homes, employment, and community services; limited availability of centralized activities; and limited options for walking or riding a bicycle (Schmidt, 2004). The low-density development associated with urban sprawl has increased reliance on the automobile for transportation. Vandegrift and Yoked (2004) assert that new location patterns produced by suburban sprawl are an important cause of rising obesity rates—new location patterns that make work, school, and social activities not as easily accessible by foot. Urban sprawl is associated with decreased rates of walking and biking and with increased rates of automobile travel compared to more densely populated communities (Frumkin, 2002). Analysis of county-level data from the U.S. Behavioral Risk Factor Surveillance System uncovered a relationship between the degree of sprawl within a community and weight, hypertension rates, and time spent walking. As the degree of sprawl within a county increased, time spent walking decreased, but obesity and hypertension became more prevalent (Ewing et al., 2003).

Frumkin (2002) suggests that the health costs of urban sprawl might be addressed through an urban planning approach that includes higher density, more contiguous development, preserved green spaces, mixed land uses with walkable neighborhoods, and limited road construction balanced by transportation alternatives. Frank et al. (2004) contend that mixed land use is the most important variable of the built environment related to obesity, and that the likelihood of obesity appears to decline with increases in mixed land use and rise with increases in time spent in a car per day. A more walkable environment has been found to be associated with higher physical activity and lower obesity levels. A study by Saelens et al. (2003) showed that adult residents of high-walkability neighborhoods, as reported by higher residential density, land use mix, street connectivity, aesthetics, and safety, engaged in more physical activity and had a lower prevalence of obesity than did residents of low-walkability neighborhoods.

Some researchers are hesitant to establish a conclusive cause-effect relationship between sprawl and obesity, suggesting other factors that might contribute to obesity (Schmidt 2004). It is difficult to make inferences about childhood activity from the available data. A primary source of statistics on average body weights in the U.S., the CDC National Health and Nutrition Examination Survey (NHANES), does not provide contextual information about physical environments (Schmidt 2004). While data linking the built environment to obesity are beginning to emerge, significant methodologic and etiologic research remains to be conducted to clarify the effect of sprawl on obesity rates.

Community Type and Location. Community type and infrastructure are other aspects of location that may be tied to obesity in both children and adults. Chatrath et al. (2002) evaluated the physical fitness of inner-city children between the ages of 4 and 18 by comparing treadmill exercise endurance times to a standard reference for treadmill performance by children. Compared to children in the reference population, who grew up in a much smaller Canadian town, the U.S. study group had significantly lower exercise endurance times, signifying poor physical fitness. A strong inverse relationship was detected between endurance time and body mass index (BMI), indicating that obesity is clearly detrimental to physical fitness. Based on these results, the authors suggested that there is a "fitness crisis" among children in urban areas of the U.S. (Chatrath et al., 2002).

Studies of adult residents in the U.S. and abroad have focused on more specific aspects of community infrastructure, including the ability of residents to walk to work and the features of neighborhoods that can promote or discourage outdoor activity. Many new residential areas are built under the assumption that the automobile is the primary means of travel, encouraging sedentary living habits (Jackson and Kochtitzky, 2001). Frank et al. (2004) evaluated the relationship between measures of the built environment in a resident's immediate neighborhood and methods of transportation, BMI, and obesity across four gender/racial classifications (white male, white female, black male, and black female). As reported walking distance and mixed land-use within the neighborhood increased, the likelihood of obesity decreased. Conversely, time spent in an automobile was positively associated with increased obesity risk. These associations, while significant across all gender and ethnicity categories, were stronger among white than black subjects (Frank et al., 2004).

A Canadian study used observational neighborhood data and information on walking to work from the 1996 Canadian Census to investigate the relationship between neighborhood infrastructure and pedestrian activity. Neighborhoods were evaluated based on an environmental score, which used a ten-point scale to rank 18 neighborhood characteristics such as the availability of walking routes, the degree of traffic threats, the mix of facilities in the area, and visual aesthetics. A significant association was found between environmental score and the percentage of people who walked to work, regardless of education level, income, and poverty rate (Craig et al., 2002). An Australian study also demonstrated the influence of community infrastructure on overweight and obesity rates. Poor pedestrian access was related to overweight, and inadequate access to recreational areas was associated with obesity. The perception of no shopping areas within walking distance was also related to obesity (Giles-Corti et al., 2003). Such results underscore the impact of an infrastructure that supports multiple activities within a community, allowing residents to walk to schools, shops, recreational areas, and workplaces.

Most of the studies on obesity in the U.S. have focused on urban or suburban populations; however, evidence suggests that obesity is widespread in rural communities, as well. Data from the 1998 National Health Interview Survey were used to study obesity and physical activity levels in rural populations. Obesity was found to be more prevalent among rural than urban adults, particularly among male residents, those without a high school diploma, and those with poor health, physical limitations, or a history of smoking. This relationship remained constant across all ethnic/racial categories. Rural residents were also more likely to lead physically inactive lifestyles than urban residents (Patterson et al., 2004).

Traffic and Pedestrian/Bicycle Access. Closely tied to community location is the volume of traffic common to a neighborhood; limited evidence suggests that traffic volume is an important factor influencing residents' physical activity. A Canadian study investigating the relationship between neighborhood characteristics and the percentage of residents who walk to work found that the perception of threats from area traffic contributed significantly to a neighborhood's environmental score (Craig et al., 2002).

The issue of pedestrian and bicycle access to recreational, educational, and retail destinations is receiving more attention as urban areas continue to become less centralized. A review of the effects of urban sprawl on neighborhood schools reported that only one out of eight children in the U.S. walks or rides a bike to school (Beaumont and Pianca, 2000). Data from the 2001 Department of Transportation National Household Travel Survey indicate that trips to school by foot or bicycle have decreased by 50% since 1969, while walking trips by children in general have declined by 60% since 1977 (Schmidt, 2003).

According to the National Trust for Historic Preservation, public policies directly contribute to these statistics. For example, the acreage standards for schools set by state and local government agencies frequently range from 10 to 60 acres, requiring new schools to be built in remote, open areas that are inaccessible by foot or bicycle (Beaumont and Pianca, 2000). A change in the walkability of newer schools is supported by the results of a study in South Carolina which found that students were four times more likely to walk to schools built before 1983 than to those built more recently (Jackson and Kochtitzky, 2001).

Several researchers have attempted to identify the neighborhood dynamics that influence walking or cycling patterns and the association between these influences and health outcomes. Craig et al. (2002) reported that factors such as secure bicycle parking, the availability of continuous walking routes, and the ability of walking routes to meet the needs of pedestrians were all significantly related to environmental score. In turn, environmental score was strongly related to the likelihood that residents walked to work in a particular community. An Australian study examining factors that lead to overweight and obesity in adults found that the perception of no bicycle or walking paths in the immediate vicinity of the home, as well as poor access to sidewalks, was linked to being overweight. Poor sidewalk access was also tied to obesity in this study, though the association was insignificant (Giles-Corti et al., 2003). In a study of American adults, Brownson et al. (2001) found a positive association between physical activity and neighborhood characteristics, including the presence of sidewalks, enjoyable scenery, heavy traffic, and hills. Timperio et al. (2004) examined associations between perceptions of the local

neighborhood and walking and cycling among children. Children's perceptions of traffic volume, road safety, and availability of public transport and parks or sporting grounds near their homes, as well as their perceptions of their parents' views on these issues, were found to influence their likelihood of walking or cycling in the neighborhood (Timperio et al., 2004).

Recreational Facilities/Playground Equipment. Limited studies have addressed the impact of access to recreational facilities or playground equipment on physical fitness. A cross-sectional survey of conditions contributing to obesity and overweight in Perth, Australia, utilized Geographic Information Systems (GIS) to assess distance between survey respondents' homes and eight recreational facilities (e.g., gyms, swimming pools, golf courses, beaches) in the area. Poor access to at least four of these recreation areas was positively associated with obesity among those surveyed (Giles-Corti et al., 2003). In a study of 1,796 adults in six counties in North Carolina, neighborhood characteristics, particularly the presence of trails and access to places for physical activity, were positively associated with leisure activity levels (Huston et al., 2003). Schmidt (2003) reported a strong correlation between activity levels among 4-year-old children and time spent outdoors and access to recreational areas such as playgrounds, parks, and yards. Contrary findings were made by Burdette and Whitaker (2004), who determined that no association existed between proximity to playgrounds and the incidence of overweight in preschoolers in a study of 7,020 low-income children.

Neighborhood Safety/Crime Rates/Violence. Several studies were identified in this literature review that assessed the relationship between security and safety in a community and outdoor physical activity among its residents. Research appears to indicate that the lack of a safe place to exercise and fears about safety are important perceived barriers to physical activity. For example, perceptions of safety and good lighting are elements of the built environment reported to be linked to physical activity (Schmidt, 2003). Greater physical activity is reported to be associated with higher perceived levels of neighborhood safety, particularly among the elderly and racial or ethnic minorities (Jackson and Kochtitzky, 2001). However, inconsistent results between some studies indicate that additional information is needed on specific neighborhood safety factors that may influence obesity.

The importance of neighborhood safety was highlighted in a review of research on obesity in minority populations by Fitzgibbon and Stolley (2004). The authors reported that a positive relationship exists between safe access to recreational facilities and physical activity, yet minority parents are twice as likely as white parents to view their neighborhoods as unsafe (Fitzgibbon and Stolley, 2004). Data from a longitudinal study of families and neighborhoods in Chicago, Illinois, were used to investigate associations between the physical activity levels of urban children and neighborhood characteristics (Molnar et al., 2004). The study included individual level physical activity data from 1,378 children in 80 urban neighborhoods, and neighborhood level data (e.g., general safety, designated areas for playing out of street, distance to play areas, community crime, vandalism, litter) from surveys of 8,782 residents and videotapes of 15,141 blocks. Lower physical activity levels were associated with the perception that a community was unsafe and that potentially threatening adult behaviors, such as fighting, prostitution, and selling drugs, were common in the neighborhood (Molnar et al., 2004). Burdette and Whitaker (2004) assessed low-income preschool children in Cincinnati, Ohio, to determine if environmental factors such as proximity to playground and fast food restaurants and

neighborhood safety affected the tendency of these children to be overweight. In contrast to the previous studies mentioned, Burdette and Whitaker found no relationship between the level of neighborhood crime and overweight conditions among these children.

3.5.5 Behavioral/Socioeconomic Factors Affecting Obesity And Physical Development

Though external factors may play a significant role in the spread of obesity, becoming overweight is largely dependent on personal behavior. In addition to neighborhood characteristics, Brownson et al. (2001) reported personal barriers to physical activity, including lack of time, feeling too tired, and no motivation to exercise. In addition to physical activity levels, which determine energy output, dietary factors appear to play a major role in the obesity epidemic. While causality has yet to be established, there is evidence that portion size and the widespread availability of energy-dense fast foods and processed snacks are fueling the rise in obesity. Learned behaviors influence eating habits, as well. For example, parental demands that children "clean their plate" may condition a child to continue eating even after they are satisfied, which could eventually lead to weight gain (Schmidt, 2003).

Socioeconomic factors have also been suggested as potential contributors to obesity. As discussed in Section 3.5.2, the prevalence of obesity among children of certain minority ethnic groups currently exceeds 25% (Schmidt, 2003). King et al. (1992, as cited in Fitzgibbon and Stolley, 2004) reported that less educated individuals and those with lower socioeconomic status were less likely to exercise than more educated people of higher socioeconomic status. Fitzgibbon and Stolley (2004) proposed explanations for these relationships, such as the wide availability of inexpensive fast food in minority communities and the rarity of leisure-time physical activity in minority households. One study found that race, education, and income were strongly correlated with perceived neighborhood environmental factors and access to places for physical activity (Huston et al., 2003). This finding suggests that people of higher socioeconomic status may have greater access to places for physical activity than lower income residents and minorities, contributing to the disparity in obesity rates among ethnic groups.

A disproportionate effect of sprawl on minority populations has not been found, although national surveys report less physical activity and higher mean body indices among Mexican-Americans and blacks than among whites (Frumkin, 2002). Current and future research may provide a more complete understanding of the relationships among neighborhood environmental factors and physical activity with regard to race.

3.5.6 References for Section 3.5

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4.0 DISCUSSION: SUMMARY AND RECOMMDATIONS FOR POTENTIAL VARIABLES FOR INCLUSION IN THE NCS

This review provides the NCS program office with a broad overview of the housing- and neighborhood-related literature in the children's health arena, with a focus on factors that may influence the health outcomes included in the NCS core hypothesis. It was intended to provide the NCS program office with a compilation of housing and neighborhood factors and conditions that warrant further investigation as candidates for measurement in the NCS. This section provides initial recommendations on the relative importance of the different candidate housing and neighborhood risk factors, based on a qualitative assessment of the literature review findings, and in relation to current study objectives and hypotheses. Section 4.1 first discusses the limitations of the review. Section 4.2 then provides the criteria used for ranking and assessing the relative importance of the different risk factors, the results of the assessment, and overall conclusions

4.1 LIMITATIONS OF THE LITERATURE REVIEW

The search strategies employed in this literature review were chosen to provide comprehensive information, but the overall scope was also limited by resources. Therefore, as with any literature review, the search strategy may not have identified all relevant articles. Another limitation of this literature review was that the literature search included only articles published after 1999. The decision to focus on the recent literature was based on time and resource constraints. As noted previously however, if the papers identified in the literature search referenced older works with widely accepted or validated results, they were also included.

It is important to note that this review has not systematically assessed the quality of the studies nor attempted a meta-analytic approach to assessing the consistency of conclusions stated in the literature. Therefore, recommendations and conclusions are based only on a qualitative assessment of the overall findings represented by the peer-reviewed literature that was identified.

Priority rankings were assigned strictly on a relative basis.

4.2 ASSESSMENT OF FINDINGS AND RECOMMENDATIONS FOR HOUSING AND NEIGHBORHOOD FACTORS FOR INVESTIGATION IN THE NCS

4.2.1 Criteria for Assessing Priority

The following criteria were used to help assess the **relative priority** of one risk factor versus another for recommendation for inclusion in the NCS.

Scientific Evidence of Potential Effect on Children's Health. The first criterion to be considered is whether the scientific literature supports the hypothesized potential impact of the risk factor on a health outcome of interest to the NCS. For example, the negative effects of environmental tobacco smoke exposure on asthma have been well established in the peer-reviewed literature. Scientific support includes papers supporting an association based on not only empirical evidence from clinical or epidemiologic studies, but also evidence based on a

scientific assessment of plausibility from a biological, physiologic, social or other analysis. It is important to acknowledge that the quantity of literature on a given housing or neighborhood factor does not necessarily reflect the relative importance or prevalence of that factor, or the magnitude of its impact on a given children's health outcome. In particular, a mature area of research would typically be supported by a much more substantial body of literature than an emerging issue, even though the emerging issue may be vastly more important in terms of impact on children's health. The quantity of published literature on a given housing or neighborhood factor is also often a reflection of policy (e.g., indicating the level of government funding for such research), rather than scientific merit. These concerns are addressed, at least partially, by the other criteria. Given these limitations, the risk factors were rated relative to the strength of scientific evidence of potential effect on the following scale:

H	Relatively strong evidence in the literature for an association (numerous peer-reviewed studies identified that found strong evidence of an association)
M	Suggestive/very limited evidence in the literature for an association (relevant studies identified were limited in number or size)
L	Inadequate or insufficient evidence in the literature to make a good scientific assessment of the plausibility of an association

Potential Impact of Improved Knowledge on Children's Health. While the first criterion assesses the likelihood that the hypothesized risk factor might be related to a health outcome, the second criterion considers the likely impact that improved knowledge of the risk factor might have on children's health. This would take into account the degree to which the risk factor is hypothesized to account for different health effects and the prevalence and severity of those health effects. For example, although the linkages between exposure to environmental tobacco smoke and numerous adverse health outcomes have been well established, additional longitudinal information on this exposure would likely have minimal impact on children's health. This does not rule out, however, that the risk factor may be a critical measure that needs to be included in the NCS as a covariate (see "Critical Measures" discussion below). The risk factors were rated relative to the strength of scientific evidence of potential impact on the following scale:

H	Literature suggests that the risk factor is or could be a major independent determinant of the health effect, and the prevalence or severity of the impacted health effect is highly significant relative to other studied effects.
M	Literature suggests that the risk factor is one of several potential determinants of the health effect, and the prevalence or severity of the impacted health effect is significant relative to other studied effects.
L	Literature suggests that the risk factor is one of many potential determinants of the health effect, with significant uncertainty as to its independent impact, or that the prevalence or severity of the impacted health effect is of lesser significance relative to other studied effects.

Appropriate for the NCS Study Design. This criterion assesses whether exploration of the hypothesized risk factor is appropriate for the large, longitudinal, mulifactorial study design of the NCS. For example, if a risk factor's association with a health effect is well-established and the public health need is for understanding the effectiveness of different interventions, then the NCS may not be the appropriate study to examine the risk factor. Conversely, if the risk factor is

potentially significant and the hypothesized mechanism of exposure can only be examined in a longitudinal study that captures exposure over time or important interactions over time, then the NCS might be uniquely suited for assessing the risk factor. Again, the risk factors were rated on a scale of *High, Medium, or Low* relative to the degree to which the expected NCS study design will be able to provide the information that is required to advance the scientific understanding of the risk factor and opportunities for mitigation.

Critical Measure for an NCS Core Hypothesis. This criterion assesses whether the risk factor represents a measure that, without which, a current NCS core hypothesis, cannot be assessed. There are two types of critical measures:

Primary (PRI)	Risk factors or exposure measurements that are specifically called out for assessment in a core hypothesis statement (for example, pesticide exposure)
Covariate (COV)	Risk factors or exposure measurements that are absolutely critical to account for in order to address other exposures in a core hypothesis (for example, ETS as a covariate in assessing the effect of indoor VOCs on asthma)

The bar is set relatively high for assigning a risk factor as a critical measure.

Measure that Places No Additional Burden on the NCS Cohort. This criterion allows for boosting a risk factor's priority ranking if it places no additional participatory burden on the NCS cohort. For example, information such as neighborhood socioeconomic status and crime rates can be gathered from governmental census and other sources and requires no direct contact with the cohort. Risk factors such as these thus have an additional advantage for inclusion. It is important to note, that while this criterion allows ease of collection to be a favorable factor in recommending inclusion, there is no attempt in this assessment to rank risk factors more broadly based on the likely cost, burden, or complexity of measuring the risk factor.

Table 4.2-1 provides the results of applying the above five criteria to each of the primary NCS core hypotheses health outcome categories, followed by an overall recommendation of the relative priority of the risk factor for inclusion in the NCS.

Table 4.2-1. Information for Setting Priorities for Measurement of Housing/Neighborhood Risk Factors in the NCS

RISK FACTORS	OUTCOME CATEGORIES																												OVERALL RECOMMENDATION
	1: Pregnancy and Birth						2: Neuro/ Behavorial/ Mental Health						3: Injury						4: Asthma/Respiratory Outcomes						5: Obesity/ Physical Development						
	Evidence of Effect	Knowledge of Impact	Appropriate NCS Measure	Critical Burden	No Cohort		Evidence of Effect	Knowledge of Impact	Appropriate NCS Measure	Critical Burden	No Cohort		Evidence of Effect	Knowledge of Impact	Appropriate NCS Measure	Critical Burden	No Cohort		Evidence of Effect	Knowledge of Impact	Appropriate NCS Measure	Critical Burden	No Cohort		Evidence of Effect	Knowledge of Impact	Appropriate NCS Measure	Critical Burden	No Cohort	
HYPOTHESIZED STRUCTURAL & PHYSICAL RISK FACTORS																													
Structure & condition							M	M	H[1]				H	H	L	COV			M	M	M								Medium Priority (primarily covariate information)
Electrical system																													Low Priority
Fire Related Factors													H	H	L														Low Priority
Building Materials							*See "Lead" row*						M	M	M[1]	COV			M	M	H[1]								Low Priority (primarily covariate information; can be replaced by other specific measures)
HVAC													M	M	L				M	M	H[1]	COV							Medium Priority (primarily covariate information; easily added housing measure)
Moisture							M	M	H[1]										H	H	H[1]	COV							High Priority (critical covariate and contributing risk factor)
Cleanliness							L	M	H[1]										M	M	H[1]	COV							Medium/High Priority (critical covariate)

Key: H = High; M = Medium; L = Low; PRI = Primary Measure; COV = Covariate

[1] Due to the ability of the NCS to adequately account for other risk factors and interactions that would reduce the power of a smaller study

[2] Relevant to endocrine disruption under obesity/physical development hypotheses

[3] Based on the number of people exposed

[4] Depends of the chemical: e.g., PCBs – high, PBDEs – low

[5] Based on literature associating general neighborhood characteristics with pre-term birth (i.e., because these variables are important components of the general neighborhood attributes)

[6] Covariate due to maternal stress linkage

RISK FACTORS	OUTCOME CATEGORIES																													OVERALL RECOMMENDATION
	1: Pregnancy and Birth							2: Neuro/ Behavorial/ Mental Health							3: Injury							4: Asthma/Respiratory Outcomes							5: Obesity/ Physical Development						
	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	
Safety devices																	H	H	L																	Low Priority
HYPOTHESIZED CHEMICAL RISK FACTORS																																				
Pesticides	M	M	H[1]			M	M	H[1]	PRI		H	M	H[1]	PRI		L	M	H[1]			L	M[2] H	[1]	PRI[2]		High Priority
Other organic chemicals	H	L[3] H	[1]			M[4]	M	H[1]								L	M	H[1]	PRI		L	M	H[1]	PRI		High Priority
Combustion by-products	L	L[3] H	[1]			L	M	H[1]			M	M	L			L	M	H[1]	PRI							High Priority
Lead	M	M	H[1]			H	H	H[1]	COV		H	M	H[1]	PRI							L	M	H[1]	PRI		High Priority
Other inorganic chemicals						M[4]	M	H[1]													L	M	H[1]	PRI		High Priority
Also see "Ambient air pollution" and "Traffic" under External Factors Affecting Housing																																				
HYPOTHESIZED BIOLOGICAL RISK FACTORS																																				
Multiple allergens																	H	H	H[1]	PRI							High Priority

Key: H = High; M = Medium; L = Low; PRI = Primary Measure; COV = Covariate

[1] Due to the ability of the NCS to adequately account for other risk factors and interactions that would reduce the power of a smaller study

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RISK FACTORS	OUTCOME CATEGORIES																													OVERALL RECOMMENDATION
	1: Pregnancy and Birth							2: Neuro/ Behavorial/ Mental Health							3: Injury							4: Asthma/Respiratory Outcomes							5: Obesity/ Physical Development						
	Evidence of Effect	Knowledge Impact of	Appropriate NCS	Measure Critical	Burden No Cohort			Evidence of Effect	Knowledge Impact of	Appropriate NCS	Measure Critical	Burden No Cohort			Evidence of Effect	Knowledge Impact of	Appropriate NCS	Measure Critical	Burden No Cohort			Evidence of Effect	Knowledge Impact of	Appropriate NCS	Measure Critical	Burden No Cohort			Evidence of Effect	Knowledge Impact of	Appropriate NCS	Measure Critical	Burden No Cohort		
Dust mites (allergens)																						H	H	H[1]	PRI										High Priority
Cockroaches (allergens and disease vectors)																						H	H	H[1]	PRI										High Priority
Mice																						M	M	M[1]	COV										Medium Priority (important covariate)
Molds							L	M	H[1]													H	H	H[1]	PRI										High Priority
Pets																						M	M	M[1]	COV										Medium Priority (important covariate; easily measured)
Bacteria, endotoxins, microbial VOCs	L	M	H[1]																			M	H	H[1]	PRI										High Priority
Other triggers (e.g., viral agents)	L	M	H[1]																			M	H	H[1]	PRI										High Priority
HYPOTHESIZED EXTERNAL FACTORS AFFECTING HOUSING & NEIGHBORHOOD RISK FACTORS																																			
Location	M[5]	M[5] H	[1]		√		H	H	H[1]		√		H	H	L	COV	√		M	M	H[1]	COV	√		M	H	H[1]	PRI	√							High Priority (easily measured; no burden on cohort; critical measure)

Key: H = High; M = Medium; L = Low; PRI = Primary Measure; COV = Covariate

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[2] Relevant to endocrine disruption under obesity/physical development hypotheses

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[6] Covariate due to maternal stress linkage

RISK FACTORS	OUTCOME CATEGORIES																												OVERALL RECOMMENDATION
	1: Pregnancy and Birth						2: Neuro/ Behavorial/ Mental Health						3: Injury						4: Asthma/Respiratory Outcomes						5: Obesity/ Physical Development						
	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	Evidence of Effect	Knowledge	Impact of	Appropriate	NCS	Measure	Critical	Burden	No Cohort	
Housing age, type & crowding							M	M	H [1]		√	H	H	L	COV	√	H	H	H[1]	P R I	√	M	H	H[1]		√	High Priority (no burden on cohort, easily measured, critical covariate)									
Zoning, sprawl, building codes							L	M	H [1]		√											M	M	H[1]	PRI	√	Medium Priority (no burden on cohort)									
Ambient air pollution	H	H	H[1]		√		L	M	H [1]		√							H	H [1]	PRI							High Priority (no burden on cohort)									
Traffic	M[5] M	[5] H	[1]		√	*See "Noise" row*						H	H	L	COV	H √	M	H	H [1]	COV	√	L	M	H [1]	PRI	√	High Priority (no burden on cohort)									
Noise	M[5] M	[5] H	[1]				M	M	H [1]											COV [6]							Medium Priority									
Crime rates, violence, neighborhood safety	M[5] M	[5] H	[1]		√		M	H	H [1]		√									COV [6]	√	M	H	H [1]	PRI	√	High Priority (no burden on cohort)									
Recreational facilities, playground equipment													H	L	COV								M	H [1]	PRI	√	High Priority (no burden on cohort)									
Pedestrian and bicycle access												M	H	L	COV							M	M	H [1]	PRI	√	High Priority (no burden on cohort)									
Water hazards												M	H	L	COV												Low Priority									

Key: H = High; M = Medium; L = Low; PRI = Primary Measure; COV = Covariate

[1] Due to the ability of the NCS to adequately account for other risk factors and interactions that would reduce the power of a smaller study

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RISK FACTORS	OUTCOME CATEGORIES: 1: Pregnancy and Birth					2: Neuro/ Behavorial/ Mental Health					3: Injury					4: Asthma/Respiratory Outcomes					5: Obesity/ Physical Development					OVERALL RECOMMENDATION
	Evidence of Effect	Impact of Knowledge	Appropriate NCS	Critical Measure	No Cohort Burden	Evidence of Effect	Impact of Knowledge	Appropriate NCS	Critical Measure	No Cohort Burden	Evidence of Effect	Impact of Knowledge	Appropriate NCS	Critical Measure	No Cohort Burden	Evidence of Effect	Impact of Knowledge	Appropriate NCS	Critical Measure	No Cohort Burden	Evidence of Effect	Impact of Knowledge	Appropriate NCS	Critical Measure	No Cohort Burden	
HYPOTHESIZED BEHAVIORAL & SES RISK FACTORS																										
Socioeconomic mediators	M[5] M	[5] H	[1]	COV		H	H	H[1]	COV		H	H	H[1]	PRI		H	H	H[1]	PRI		H	H	H[1]	PRI		High Priority
Environmental Tobacco Smoke				COV					COV										COV					COV		High Priority

Key: H = High; M = Medium; L = Low; PRI = Primary Measure; COV = Covariate
[1] Due to the ability of the NCS to adequately account for other risk factors and interactions that would reduce the power of a smaller study
[2] Relevant to endocrine disruption under obesity/physical development hypotheses
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[6] Covariate due to maternal stress linkage

4.2.2 Overall Conclusions

This literature review attempts to frame an overview of key attributes of housing and neighborhoods in terms of their potential relative importance for the NCS. To proceed with the process of determining which factors will ultimately be most important and feasible for the NCS, critical questions such as cost, burden, and how and when these risk factors will be measured, must be addressed. These issues, as well as approaches for integration of key housing and neighborhood assessments into the overall NCS study design, are discussed in a companion report, "Fourth Interim Report: Literature Search on Measurement of Housing and Neighborhood Quality Related to Child Health and Development."

Other major conclusions of this review are as follows:

1) Measurement of risk factors associated with housing and neighborhoods will be critical to the assessment of multiple NCS hypotheses

2) The NCS will require significant costs to adequately characterize residential exposures that must be measured to address hypotheses related to asthma, neurodevelopmental effects, and endocrine disruption.

3) Many housing and neighborhood risk factors can be measured with little or no additional burden on the cohort, and may only require a one-time measurement – a significant benefit of their inclusion; however, although a risk factor may be easily measured, its effect on child health and development over time may be difficult or impossible to estimate.

4) The NCS provides a unique opportunity to account for many different exposures simultaneously and therefore assess timing and interactions that can shed significant light on the impact of complex residential exposure scenarios.

APPENDIX A

HYPOTHESES FOR THE NATIONAL CHILDREN'S STUDY

HYPOTHESES FOR THE NATIONAL CHILDREN'S STUDY (Source: Appendix F: Draft White Paper on Measures for NCS Core Hypotheses, prepared by Battelle (February 20, 2004) for discussion at a sample design workshop.)

1.0 Undesirable outcomes of pregnancy: birth defects and preterm birth

1.1 Among women without diabetes before pregnancy, impaired glucose metabolism during pregnancy is proportional to risk of major congenital malformations of the heart, central nervous system, musculoskeletal system, and all birth defects combined

1.2 Intrauterine exposure to mediators of inflammation due to infection of either vaginal, cervical, or uterine sites, or of more distal sites (e.g., periodontal disease) is associated with an increased risk of preterm birth.

2.0 Altered neurobehavioral development, developmental disabilities, and psychiatric outcomes

2.1 Repeated low-level exposure to nonpersistent pesticides in utero or postnatally increases risk of poor performance on neurobehavioral and cognitive examinations during infancy and later in childhood, especially, for certain agents, among those with genetically decreased paraoxonase activity.

2.2 Prenatal infection and mediators of inflammation are risk factors for neurodevelopmental disabilities, such as cerebral palsy and autism.

2.3 Infection and mediators of inflammation during pregnancy and the perinatal period are associated with increased risk of schizophrenia.

3.0 Injury

(Note: Hypotheses 3.1 and 3.2 were recently removed by the ICC but are currently being further strengthened for possible inclusion as NCS hypotheses.)

3.1 Exposures early in life that lead to neurotoxic effects are associated with increased risk of injury.

3.2 Attributes of childcare and relationship with caregivers influence risk of injury.

3.3 Repeated head trauma has a cumulative adverse effect on neurocognitive development.

4.0 Asthma

4.1 Exposure to indoor and outdoor air pollution and bioaerosols (including allergens, endotoxin, and mold) is associated with increased risk of asthma.

4.2 Respiratory viral infection early in life is associated with increased risk of asthma.

4.3 Maternal stress during pregnancy is associated with increased risk of asthma.

4.4 Antioxidant constituents of diet decrease risk of asthma.

4.5 Early exposure to bacterial and microbial products decreases risk of asthma (hygiene hypothesis).

4.6 Access to health care and management of asthma are strongly related to asthma hospitalization.

5.0 Obesity and altered physical development

5.1 Impaired maternal glucose metabolism during pregnancy is directly related to risk of obesity and insulin resistance in offspring.

5.2 Intrauterine growth restriction as determined by serial ultrasound examination is associated with subsequent risk of central obesity and insulin resistance in offspring, independent of subsequent body mass index.

5.3 Breast milk feeding, compared with infant formula feeding, and breastfeeding duration are associated with lower rates of obesity and lower risk of insulin resistance.

5.4 Dietary predictors of obesity and insulin resistance include reduced intake of fiber and whole grains, and high glycemic index.

5.5 Environmental factors such as distance to parks, availability of walking routes in the neighborhood, and neighborhood safety are associated with risk of obesity and insulin resistance.

5.6 Social, behavioral, and family factors that affect development of dietary preferences and physical activity patterns early in childhood determine risk of childhood obesity and insulin resistance.

5.7 In utero and subsequent exposure to environmental agents that affect the endocrine system (bisphenol A, atrazine, and lead) results in altered age at puberty.