

Healthy Homes Issues: Asthma Version 3

March 2006

Prepared for:

U.S. Department of Housing and Urban Development (HUD) Office of Healthy Homes and Lead Hazard Control Washington DC 20410

Prepared by:

Peter Ashley, DrPH, U.S. Department of Housing and Urban Development (HUD) John R. Menkedick, MS, Battelle Maureen A. Wooton, MS, Battelle Jennifer A. Zewatsky, MS, MEn, Battelle Steve Weitz, MA, Healthy Housing Solutions Joanna Gaitens, PhD, Healthy Housing Solutions Jack Anderson, BA, Healthy Housing Solutions

March 2006

Contracts No. C-OPC-21357 and No. C-PHI-00931

Acknowledgments

We thank the following individuals for their helpful comments and information used in preparation of this document.

Terrence M. Allan, M.P.H. Cuyahoga County Board of Health

Gary Adamkiewicz, Ph.D., M.P.H Harvard School of Public Health

Martin D. Chapman, Ph.D. INDOOR Biotechnologies, Inc.

Dorr G. Dearborn, Ph.D., M.D. Director, Swetland Center for Environmental Health Case Western University

Peter Gergen, M.D. Department of Health and Human Services Agency for Healthcare Research and Quality

Stuart Greenberg, Executive Director Environmental Health Watch

J. David Miller, Ph.D. Department of Chemistry, Carleton University

Megan Sandel, M.D., M.P.H. Boston University School of Medicine

Tim K. Takaro, M.D., M.P.H. Faculty of Health Sciences, Simon Fraser University

Preface

In 1998, Congress appropriated funds and directed the U.S. Department of Housing and Urban Development (HUD) to "develop and implement a program of research and demonstration projects that would address multiple housing-related problems affecting the health of children." In response, HUD solicited the advice of experts in several disciplines and developed a preliminary plan for the Healthy Homes Initiative (HHI). The primary goal of the HHI is to protect children from housing conditions that are responsible for multiple diseases and injuries. As part of this initiative, HUD has prepared a series of papers to provide background information to their current HHI grantees, as well as other programs considering adopting a healthy homes approach. This background paper focuses on asthma and provides a brief overview of the current status of knowledge on:

- The extent and nature of asthma triggers in the home;
- Assessment methods for asthma triggers in the home;
- Mitigation methods for asthma triggers in the home; and
- Research needs with respect to housing and asthma.

Please send all comments to:

Peter Ashley, DrPH, at: Peter_J._Ashley@hud.gov or Emily Williams, M.S., at: Emily_E._Williams@hud.gov

U.S. Department of Housing and Urban Development (HUD) Office of Healthy Homes and Lead Hazard Control Fax: 202-755-1000

Table of Contents

1.0	OVE	RVIEW OF ASTHMA AND THE HOME ENVIRONMENT	1
2.0	EXT	ENT AND NATURE OF ASTHMA TRIGGERS IN THE HOME	4
	2.1	Dust Mite Allergens	6
	2.2	Cockroach Allergens	
	2.3	Pet and Rodent Allergens	
	2.4	Molds	
	2.5	Indoor Chemical Air Pollutants	
3.0	MET	HODS OF ASSESSING ASTHMA TRIGGERS IN THE HOME	13
	3.1	Environmental Sampling and Analysis	17
	3.2	New Techniques for Home Testing	
	3.3	Interpretation of Results	
4.0	MET	HODS BEING USED TO MITIGATE ASTHMA TRIGGERS IN THE HOME .	25
	4.1	Dust Mite Allergens	30
	4.2	Cockroach Allergens	
	4.3	Pet and Rodent Allergens	
	4.4	Molds	
	4.5	Indoor Chemical Air Pollutants	
5.0	CUR	RENT RESEARCH AND INFORMATION GAPS	39
Refer	ences		41
Appe	ndix A:	Additional Internet Resources	55

List of Tables

Table 1.	Summary of NAS Findings Regarding the Association Between Biological and Chemical Exposures in the Home and the Development and Exacerbation of Asthma in Sensitive Individuals
Table 2.	Overview of Assessment Strategy Options for Selected Residential Asthma Triggers15
Table 3.	Current Threshold Levels for Assessing Common Residential Allergens
Table 4.	Summary of Recent Multi-faceted Environmental Intervention Studies
Table 5.	Major Mitigation Methods and Asthma Triggers Potentially Affected30

Healthy Homes Issues: Asthma

1.0 OVERVIEW OF ASTHMA AND THE HOME ENVIRONMENT

More than 20 million people in the United States are estimated to have asthma (CDC, 2003). 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, 1998b; Carter and Platts-Mills, 1998; Platts-Mills, 1998). Furthermore, in the U.S., rates of increase of asthma are disproportionately high among children and African Americans (Eggleston, 2000). Although research has suggested that a large portion of the observed racial/ethnic differences in asthma prevalence is explained by factors related to income and level of education (Litonjua et al., 1999), residence in an urban area has been implicated as an important risk factor for all children (Aligne et al., 2000). Researchers have also 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). However, substantial differences in the overall burden of agents which exacerbate asthma have not necessarily been established (Kitch, 2000).

These increases in asthma prevalence and severity have occurred despite general reductions in levels of most air pollutants outside; therefore, many researchers instead point to coinciding changes in the home environment as potentially influential, and possibly more important, factors in determining asthma risk (Custovic et al., 1998). In particular, housing designs intended to increase energy efficiency, resulting in a decrease in passive ventilation, and the presence of upholstered furnishings and carpeting 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 (Platts-Mills et al., 1997; Platts-Mills, 1998; Carter and Platts-Mills, 1998; Custovic et al., 1998). Potentially increasing the significance of indoor air exposures as risk factors for asthma, data show children in the U.S. currently spend the overwhelming majority of their time indoors (USEPA, 1997a).

The strongest established risk factors for development of asthma are family history of allergic disease and sensitization to one or more indoor allergens. Allergens are proteins with the ability to trigger immune responses and cause allergic reactions (atopy) in susceptible individuals (e.g., those with a family history of allergic disease). They are typically found adhered to very small particles, which can be airborne as well as present in household dust reservoirs (e.g., in carpets and on surfaces). In indoor environments, allergen exposure primarily occurs through inhalation of allergens associated with airborne particles. Common indoor allergen sources include dust mites, cockroaches, animals (domestic animals and pests such as rodents), and mold. Particular allergens identified in animals include proteins found in the urine (for rodents), saliva (for both cat and cockroaches), feces (for house dust mites and cockroaches), and skin flakes or body casing particles (for dog, cat, and cockroach) (Erwin, et al., 2003; Katial, 2003). Conventionally speaking, sensitization to a substance is the development of the potential for an allergic reaction to that substance. Sensitization occurs in susceptible individuals when repeated exposure to an allergen (also called an antigen in immunological science) results in the production of the

immunoglobulin E (IgE) antibody. An antibody is a protein that is manufactured by lymphocytes (a type of white blood cell) to neutralize an antigen or foreign protein. An allergic response may result when the individual is again exposed to the substance which caused IgE antibody formation. IgE is a class of antibody normally present in very low levels in humans but found in larger quantities in people with allergies and certain infections. Evidence suggests that it is the primary antibody responsible for the classic allergic reaction (American Academy of Allergy, Asthma and Immunology (AAAI), <u>http://www.aaaai.org/</u>).

Of the tests used to determine whether an individual is sensitive to an allergen, the skin prick is the most common method. A small amount of allergen is introduced into the skin by making a small puncture through a drop of allergen extract. Swelling occurs if the patient is allergic to the specific allergen. If skin-prick tests are all negative, a physician may use a more sensitive, but less specific intradermal test. Generally, intradermal testing is used to test for allergy to insect stings or penicillin (Li, 2002). A blood test, called a RAST (radioallergosorbent) test, may sometimes be used. This is a more expensive method, is generally less sensitive than skin testing, and requires more time for results to be available. It is generally used only when skin tests cannot be performed. Allergen extracts are produced commercially according to Food and Drug Administration (FDA) standards.

Exposure to house dust mite allergens in childhood has been linked to an increase in the relative risk of developing asthma, and numerous other allergens are associated with asthma exacerbation in sensitized individuals (NAS, 2000). Asthma exacerbation is the onset or worsening of symptoms, such as shortness of breath, cough, wheezing, and chest tightness, in an individual who has already developed asthma. Data regarding critical ages for sensitization are not well defined in the literature. Research does generally support the recommendation that avoidance measures for allergens be introduced before birth or at the earliest possible age in high-risk infants (e.g., those with family histories of allergic diseases, atopic dermatitis in the first three months of life, or sensitizations to specific food allergens in the first three years of life) (Bergmann et al., 1998). In the Canadian Childhood Asthma Primary Prevention Study, intervention (which included encouragement of breast feeding as well as environmental measures) began during the third trimester of pregnancy and continued for the first year of life. Environmental measures consisted of (1) dust mite control, including encasement of parents' and infants' beds, weekly cleaning of bedding, and treatment of carpeting and upholstery with benzyl benzoate powder and foam, respectively, (2) pet avoidance measures, and (3) avoidance of environmental tobacco smoke. At seven years after birth, the prevalence of pediatric allergistdiagnosed asthma was significantly lower in the intervention group than in the control group (14.9 % vs. 23.0%) (Chan-Yeung et al., 2005).

Nonetheless, many questions remain. For example, recent evidence has suggested that high-dose exposure to cat allergen early in life may produce a form of immunologic tolerance to cats, rather than cause sensitization (Platts-Mills et al., 2000a and 2000b; Platts-Mills et al., 2001; Ronmark et al., 2003). Furthermore, it has been suggested that avoidance of cat allergens by removing the cat from the family home, especially within a community where many other cats are present (i.e., moderate ambient levels of cat allergen are present), might achieve the opposite of the intended effect for children in the early stages of immune system development (i.e., immunologic

tolerance might have occurred at higher exposure levels; sensitization can occur at moderate levels) (Platts-Mills et al., 2000a and 2000b; Platts-Mills et al., 2001). Additional research is needed to better characterize the complex relationship between pet ownership and asthma. Specifically, intervention studies in which pets are removed from the home may help to determine the effect of animal removal on asthma development (Apter, 2003).

Another concept, known as the "hygiene hypothesis," has spawned a number of 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, and close proximity to farming practices may decrease the risk of atopy and asthma (Liu and Szefler, 2003; Alm et al., 1999; 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.

Research also indicates that other factors can exacerbate asthma symptoms, such as respiratory tract infections, bacterial endotoxins, indoor pollutants (environmental tobacco smoke, nitrogen oxides/indoor combustion products, formaldehyde, phthalates, VOCs, pesticides), outdoor pollutants that penetrate the indoor environment (sulfur oxides, ozone, particulate matter), cold air, obesity, exercise, and the presence of wood burning stoves and fireplaces. These substances act by an irritant mechanism which sets off the body's inflammatory response as opposed to the allergic mechanism described above. In the case of bacterial endotoxins, the relationship between exposure and asthma symptoms is difficult to characterize. Some studies have associated endotoxin with asthma exacerbation, while others have noted that endotoxin exposure may have a protective effect early in life. 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. Thorne et al. (2005), using cross-sectional data from 831 U.S. homes in the National Survey of Lead and Allergens in Housing, found that endotoxin levels in settled dust were significantly related to diagnosed asthma, asthma symptoms in the past year, current use of asthma medications, and wheezing, but not allergy. The relationships were strongest for dust on bedroom floors and bedding, they were observed in adults only, and they indicate that "endotoxin exposure worsens symptoms in adults, regardless of whether an individual has allergies or not." A study of children in rural Germany, Austria, and Switzerland, however, produced quite different results. In these areas, researchers found that children from

farming households who are routinely exposed to high levels of environmental endotoxin were observed to have a significantly decreased risk of hay fever, sensitization to six common aeroallergens, 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 in early life. (Braun-Fahrlander, 2003).

The few studies focusing on asthma in elderly persons indicate that it is a significant problem for this population group, that much of the cause of morbidity may be sensitivity to indoor allergens, and that the pattern of sensitivity appears to be similar to that reported in children and young adults in urban areas of the United States (Huss et al., 2001a; Rogers et al., 2002).

2.0 EXTENT AND NATURE OF ASTHMA TRIGGERS IN THE HOME

In support of the U.S. Environmental Protection Agency's (EPA) efforts to develop an asthma outreach strategy, the National Academy of Sciences' 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 assessment (IOM Report), a number of biological and chemical 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. General findings and conclusions of the assessment committee regarding the association between exposure to an indoor agent and asthma development and exacerbation are summarized in Table 1 below. Following the table, selected key studies relevant to the major indoor agents associated with asthma, and the residential factors that affect these agents, are discussed further.

In overview, the major independent risk factor that has been identified to date for asthma is dust mite sensitization; however, although the literature supports this association in many areas, the relative importance of other indoor allergens (especially in different geographical areas) is unclear. Various studies have shown that sensitization to mouse or cockroach allergens can be more or equally important in certain (e.g., urban) areas, and that risk factors can depend on the climate and the socioeconomic status of the household (Platts-Mills et al., 1997, 2000a and 2000b; Phipatanakul, 2000a and 2000b). For example, 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., 1999a; Phipatanakul, 2000a and 2000b; Gruchalla et al., 2005). In very low humidity climates in the mountains of New Mexico (i.e., where dust mites and fungi are less prevalent), sensitization to dog and cat allergens has been observed to be more strongly associated with respiratory symptoms (Sporik et al., 1995 and Ingram et al., 1995 as cited in Platts-Mills et al., 1997). The Inner City Asthma Study, which was conducted in seven metropolitan inner city areas in the United States, found that cockroach exposure and sensitivity predominated in the Northeast, whereas dust-mite exposure and sensitivity were predominant in southern and northwestern cities (Gruchalla et al., 2005). The association between allergens and asthma is further complicated by

4

Table 1. Summary of NAS Findings Regarding the Association Between Biological and Chemical Exposures in the Home and the Development and Exacerbation of Asthma in Sensitive Individuals.

Developmen	t of Asthma	Exacerbation of Asthma						
Biological Agents Chemical Agen		Biological Agents	Chemical Agents					
	Sufficient Evidence of a Causal Relationship ¹							
Dust mite	No agents met this definition	Cat Cockroach Dust mite	ETS (in preschool-aged children)					
	Sufficient Evidence of	f an Association ²						
No agents met this definition	ETS (in preschool-aged children)	Dog Fungi or mold Rhinovirus	Nitrogen oxides (high-level exposures) ³					
	Limited or Suggestive Evide							
Cockroach (in preschool-aged children) Respiratory Syncytial virus	No agents met this definition	Domestic birds Chlamydia pneumoniae Mycoplasma pneumoniae Respiratory Syncytial virus	ETS (in older children and adults) Formaldehyde Fragrances					
	Inadequate or Insufficient Whether or Not an As	Evidence to Determine	· · ·					
Cat, Dog, Domestic BirdsNitrogen oxidesRodentsPesticidesPesticidesRodentsPesticidesChlamydia trachomatisPlasticizersCockroaches (except for preschool-aged children)PlasticizersEndotoxinsVOCsVOCsHouseplantsPollenFungi or moldsFragrancesInsects other than cockroachesPolsenChlamydia trachomatisETS (in older children and adults)cockroachesPollenHouseplantsadults)PollenPollen								
Limited or Suggestive Evidence of No Association 7								
No agents met this definition No agents met this definition No agents met this definition								

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

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

⁴ 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)

⁵ 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

⁶ 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).

⁷ 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).

the issue of genetics, which is known to predispose children to asthma and related conditions. Lanphear et al. (2001) observed an association between asthma and both parental atopy and African-American race. Results from another study suggest that children may be genetically predisposed to be more or less susceptible to certain indoor pollutants (Belanger et al., 2003).

General conclusions about the comparative risk of various indoor agents associated with asthma are difficult, largely due to the dependency of the particular risk on the characteristics of a given environment (e.g., climate, urban setting) and its occupants (e.g., smokers, genetics). In addition, the literature on indoor risks associated with asthma generally focuses on single agents; in reality, however, occupants of houses receive exposures to multiple agents that may interact physically or chemically with each other or their environment, or that may act synergistically (e.g., endotoxins or diesel exhaust and various household allergens) (NAS, 2000; Pandya et al., 2002; Miller et al., 2004).

The World Health Organization/International Union of Immunological Societies (WHO/IUIS) Allergen Nomenclature Sub-Committee has developed a systematic nomenclature for describing all characterized allergens (Smith, 1999; WHO/IUIS Allergen Nomenclature Subcommittee, 1994). In this system, allergens are generally designated according to the accepted taxonomic name of their source as follows: the first three letters of the genus, followed by a blank space, followed by the first letter of the species, followed by a blank space, and finally an Arabic number. The Arabic numerals are assigned to allergens in the chronological order of their identification. For example, the first cat (*Felis domesticus*) allergen to be successfully purified is Fel d 1. Allergens isolated to date from the Dermatophagoides farinae species of dust mite include Der f 1, Der f 2, Der f 3, Der f 5, Der f 7, and Der f 10. In some instances, this nomenclature method must be modified to accommodate special cases, for example, by adding an extra letter to differentiate allergen names for species that would otherwise be ambiguous (WHO/IUIS Allergen Nomenclature Subcommittee, 1994).

2.1 <u>Dust Mite Allergens</u>

House dust mites are the only home allergen source for which the National Academies' IOM report 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). For example, in a review of studies on middle-class or mixed economic-class asthmatic children, Kattan et al. (1997) report that 50-60% of children had positive skin test results to dust mites. Huss et al. (2001b) report that analysis of early cross-sectional data from 1041 children in the Childhood Asthma Management Program (a five-year study sponsored by the National Heart, Lung and Blood Institute) show that, for house dust mites, the higher the level of allergen exposure, the more likely patients were to have positive skin test responses.

Mites are a very common exposure source in temperate and humid regions such as the southeastern United States. Based on results from the National Survey of Lead and Allergens in Housing, which had data from 831 U.S. homes and was conducted in 1998 and 1999 with

funding from HUD and NIEHS, Arbes et al. (2003a) 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. The primary determinants of dust mite growth in homes are food source (i.e., skin scales), temperature, humidity and the availability of upholstered furniture, carpets, mattresses, and pillows (Vaughan and Platts-Mills, 2000). Of these, humidity is generally the limiting factor (NAS, 2000). 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). Most dust mite exposure is thought to occur as mite fecal pellets and aggregates associated with larger (~10-25 μ m) dust particles that become airborne during and immediately after disturbance of dust reservoirs (NAS, 2000).

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).

2.2 Cockroach Allergens

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). 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 Blag 1 or 2 (i.e., less that 0.05 Units/g dust), 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). The Inner City Asthma Study found that cockroach allergens appear to have a greater effect on asthma morbidity than dust mite or pet allergens for inner-city asthmatic children with a positive skin test. Although both cockroach allergen exposure and dust mite allergen exposure were risk factors for the development of positive skin test reactions, only cockroach allergen exposure, in conjunction with cockroach sensitivity, was associated with increased asthma morbidity. The study found clear differences among the seven study sites, however, in allergen exposure and skin test reactivity. Cockroach allergens and sensitivity were predominant in northeastern cities and dust mite exposure and sensitivity were higher in the south and northwest (Gruchalla et al., 2005). Cockroaches, like dust mites, thrive in temperate and humid regions, but may also proliferate in northern states (Chapman et al., 1997).

Cohn et al. (2005), analyzing data from the National Survey of Lead and Allergens in Housing, found cockroach allergen (Bla g 1) concentrations exceeding 2.0 U/g (a level associated with allergic sensitization) in 13% of kitchen floors and 11% of living room floors nationwide.

Concentrations exceeding 8.0 U/g (a level associated with asthma morbidity) were found in 10% of kitchen floors and 3% of living room floors. Elevated concentrations were associated with high-rise buildings, urban settings, pre-1940 construction, and household incomes of less than \$20,000.

Other studies have also found 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 is in contrast to 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 prick skin 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 independent 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 substandard housing permits cockroach infestation, including rural areas, suburbs, and small towns and cities across the United States (Arruda et al., 2001). 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.

Although there are over 70 cockroach species that occur in the U.S., only five species are commonly found in residential settings: the German cockroach (*Blatella germanica*), the American cockroach (*Perplaneta americana*), the Oriental cockroach (*Blatta orientalis*), the smoky brown cockroach (*Perplaneta 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 allergen 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 tend 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).

2.3 <u>Pet and Rodent Allergens</u>

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 Report found sufficient evidence for the role of cat and dog allergen in asthma exacerbation, but not for either allergen in terms of asthma development (NAS, 2000). 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 (<10um) 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). Although a number of studies have shown 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), levels of these allergens in homes are clearly highest in homes housing these animals (Chapman and Wood, 2001). Therefore, occupant choice plays the primary role in determining indoor exposure to pet allergens.

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 μ g/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 μ g 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). 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).

The IOM Report 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 μ g/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 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.

2.4 <u>Molds</u>

There are over 200 species of fungi, including those commonly called "mold," to which people are routinely exposed indoors and outdoors. 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. Molds are thought to play a role in asthma in several ways. They are known to produce proteins that are potentially allergenic, and there is evidence of associations between fungal allergen exposure and asthma exacerbation. 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. Finally, mold toxins (mycotoxins) may cause lung damage leading to pulmonary diseases other than asthma (NAS, 2000).

In 2004, the Institute of Medicine of the National Academies published a comprehensive review of the scientific literature on the relationship between damp or moldy indoor environments and the manifestation of adverse health effects, particularly respiratory and allergic symptoms (IOM, 2004). The Institute found sufficient evidence of an association with symptoms of the upper respiratory tract (nasal and throat), asthma symptoms in sensitized asthmatic persons, hypersensitivity pneumonitis (inflammation in the lungs) in susceptible persons (i.e., persons with a family history of sensitivity), wheeze, and cough. They found limited or suggestive evidence of an association with lower respiratory illness in otherwise healthy children. However, the Institute did not find sufficient evidence of a *causal* relationship with any health outcomes, and they concluded that evidence was inadequate or insufficient to determine an association with many health effects, including asthma development, dyspnea (shortness of breath), airflow obstruction (in otherwise healthy persons), mucous membrane irritation syndrome, chronic obstructive pulmonary disease, lower respiratory illness in otherwise healthy adults, and acute idiopathic pulmonary hemorrhage in infants. These conclusions are not applicable to immunocompromised persons, who are at increased risk for fungal colonization or opportunistic infections.

While detecting allergic sensitization to molds is difficult in infants, some data suggest that infants at risk for developing allergic disease experience respiratory symptoms which may or may not be allergic in nature. In a study conducted by Belanger et al. (2003), a positive exposure-response was found 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 mold samples represented longer-term exposure concentrations, the study results suggested that the infants 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. 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 and the presence of other moisture dependant biological hazards such as endotoxins (Gent et al., 2002; Thorne et al., 2005).

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). 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 may be important as sources of mold irritants or allergens. In contrast, under wet conditions (i.e., in the presence of water-soaked cellulosic materials), toxin producing molds (e.g., *Stachybotrys chartarum*) may be prominent (Flannigan, 1997). The role of *Stachybotrys* in asthma is not known. In general, whether or not a potentially toxigenic fungus produces toxins is dependent on environmental conditions and nutrient source (Burge and Amman, 1999).

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 μ m, although some may be released as chains or clumps of spores (NAS, 2000).

Some of the major mold allergens identified and isolated to date include those from *Aspergillus funigatus* (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). 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 specific mold allergen sensitization or asthma causation remains undetermined (NAS, 2000; IOM, 2004). Information on the nature of exposures that lead to

mold-related asthma is lacking (ACGIH, 1999; 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). The clearest association between mold exposure and asthma is sensitization to *Alternaria*, 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). 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., 1999a; Kattan et al., 1997).

For further information on mold, see the HUD background paper, "Healthy Homes Issues: Mold."

2.5 Indoor Chemical Air Pollutants

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 indoor exposure to environmental tobacco smoke (ETS), formaldehyde and certain other volatile organic compounds (VOCs), phthalates (found in many plastics), some household products such as pesticides, and various combustion products (nitrogen oxides, sulfur oxides, carbon monoxide (CO)) can be related to asthmatic symptoms in susceptible individuals (Becher et al., 1996; Garrett et al., 1999; Bornehag et al., 2004). Common indoor sources of formaldehyde include particle board, plywood, paneling, certain types of foam insulation, and some carpets and furniture (Garrett et al., 1999). Phthalates are widely used as plasticizers in polyvinyl chloride (PVC) flooring, wall material, vinyl tile and vinyl toys (Bornehag et al., 2005). The primary sources of nitrogen and sulfur oxides, CO, VOCs, and particulates include tobacco smoke, vehicle start-up and idling in attached garages, and combustion appliances that are either unvented or that have improperly installed or malfunctioning ventilation. 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). A crosssectional 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., 2001). A strong relationship was also found between formaldehyde concentration and exacerbation of wheezing illness in a recent U.K. study (Venn et al., 2003).

In the National Academy of Sciences' IOM review of the available literature (NAS, 2000), there were no indoor chemical exposures that 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. Of the other indoor chemicals that were assessed in NAS review, sufficient evidence was found to support an association between high level exposures to nitrogen dioxide and asthma exacerbation, and limited evidence was found of an association between formaldehyde and

fragrance exposures and asthma exacerbation. Inadequate or insufficient evidence was available for determination of the exact role of other indoor pollutants, such as pesticides and VOCs, in asthma exacerbation or development (NAS, 2000).

Swedish researchers have reported an association between asthma and allergies in children and concentrations of n-butyl benzyl phthalate (BBzP) and di(2-ethylhexyl) phthalate (DEHP) in dust collected from the children's bedrooms (Bornehag et al., 2004). The same researchers have found associations between dust concentrations of those two phthalates and the amount of PVC used as flooring and wall material in the home. High concentrations of BBzP were associated with reported water leakage in the home, and high concentrations of DEHP were associated with buildings constructed before 1960 (Bornehag et al., 2005).

Although there is currently no conclusive evidence of a link to indoor exposure to pesticides and exacerbation of childhood asthma, limited evidence does exist for a link between pesticide exposure and asthma in adults in occupational settings (Etzel, 1995). Pesticides may be of particular concern in low-income, inner-city areas, where conditions favor pest infestation. For example, Whyatt et al. (2002) found that 85 percent of pregnant women in minority communities reported the use of insecticides during pregnancy. For further information on pesticides, see the HUD background paper, "Healthy Homes Issues: Pesticides."

Researchers in California found a link between herbicides and childhood asthma (Salam et al., 2004). While rarely an indoor source, herbicides may be an environmental problem affecting homes in some communities just as vehicle exhaust is in others.

3.0 METHODS OF ASSESSING ASTHMA TRIGGERS IN THE HOME

An overview of selected residential asthma triggers and sampling assessment strategies is summarized in Table 2. This overview, and the discussion that follows, provides the reader with an overall picture of the range of assessment technologies that are available, from both a research and programmatic perspective. The level of rigor involved in assessing asthma triggers in a research setting generally surpasses that which is needed for programmatic or public health use. From a housing or public health perspective, a home assessment is generally constrained by the need for cost-effective methods that are sufficient to allow for the identification of a substance which may be at levels of concern in the home environment.

While the discussion in this section focuses on quantitative methods, other methods such as lower cost visual inspection or questionnaires or checklists can also provide a qualitative assessment of the potential asthma hazard in a home. Visual measures such as dampness, visible mold growth, signs of cockroach or rodent activity, the presence of pets, the presence and condition of upholstery and carpets, the presence of sources of CO or VOCs, and general cleanliness, can all be used to identify particularly obvious sources of potential asthma exacerbation.

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 carpeted versus smooth 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 $\geq 10 \ \mu g/g$; 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).

Due to the uncertainties associated with interpretation of environmental samples for mold contamination, visual inspection for dampness and detection of musty odors, often obtained from occupant questionnaires, are the most frequently used methods to assess the potential for indoor mold exposure. However, visual observation is limited by the fact that fungi are microscopic and their presence is often not apparent until growth is extensive. 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. Others have had more success, however (Park et al., 2004; Mahooti-Brooks et al., 2004). Although direct observation of dampness or visible fungal growth is usually sufficient to warrant a recommendation for mitigation, further air or source sampling may be conducted for documentation purposes and to record the types of fungi that predominate (Burge and Otten, 1999).

	Assessment Strategy							
Residential	Sampling		Analysis		Test Applicability			
Trigger	Method	Reliability	Method (units)	Quality assurance	Important Species	Data Obtained ²		
Dust mite allergens	Dust sampling by vacuum	Spatially and temporally variable; most mites in settled dust	ELISA ³ (µg/g)	Accurate quantitation, sensitive	Dermatophagoides species and Blomia tropicalis	Allergen levels (Group 1 (Der p 1 * and Der f 1); Group 2 (Der p 2 and Der f 2); Blo t 5)		
			ACLOTEST® ⁴	Semi-quantitative (quicktest)	D. pteronyssinus and D. farinae	Detection of Group 2 mites sensitive to 0.5 µg/g dust		
			Gold-based lateral flow test ⁵	Semi-quantitative, sensitive (quicktest)	D. pteronyssinus and D. farinae	Allergen levels (Der p 1 * and Der f 1)		
	Air sampling with static or personal sampler	Spatially and temporally variable; also variable with disturbance	ELISA ³ (pg/m ³)	Accurate quantitation, sensitive	D. pteronyssinus	Allergen levels (Group 1 (Der p 1 * and Der f 1); Group 2 (Der p 2 and Der f 2); Blo t 5)		
	Dust or air (sampled as above)	See above	Particle immunostaining	Extremely sensitive	D. pteronyssinus	Allergen levels (Der p 1* and Der p 2)		
Cockroach allergens	Dust sampling by vacuum or air	Spatially and temporally variable; most cockroach	ELISA ³ (Units/g) (dust) ELISA ³ (Units/m ³) (air)	Accurate quantitation, sensitive	Blatella germanica and Periplaneta americana	Allergen levels (Bla g 1 and Bla g 2)		
	sampling with static or personal sampler	allergen in settled dust; air levels variable with disturbance	Particle immunostaining	Extremely sensitive	Blatella germanica	Allergen levels (Bla g 1)		
	Trapping		Cockroach counts		Nonselective	Estimates of cockroach population		
Pet and rodent allergens	Dust sampling by vacuum or air sampling with static	Spatially and temporally variable; variable with disturbance; high levels of pet	ELISA ³ (μg/g) (dust) ELISA ³ (pg/m ³) (air)	Accurate quantitation, sensitive	Felis domesticus, Canis familiaris, Mus musculus	Allergen levels (Fel d 1, Can f 1 * , Mus m 1, Rat n 1 (rat urine))		
	or personal sampler	allergen airborne	Particle immunostaining	Extremely sensitive	Canis familiaris and Felis domesticus	Allergen levels (Can f 1 * and Fel d 1)		

Table 2. Overview of Assessment Strategy Options for Selected Residential Asthma Triggers ¹

¹ See text for references.

² Allergens listed in this column are those for which monoclonal antibodies are typically commercially available for immunoassay purposes (see INDOOR Biotechnologies website, <u>http://www/inbio.com/index.html</u>)

³ Quantitative differences between allergen standards are currently an important source of assay (ELISA) variability.

⁴Additional information on ACLOTEST® is available on the internet from the Allergy Buyers Club, <u>http://store.yahoo.com/allergybuyersclub/dustmitetestkit.html</u>.

⁵ Additional information on the gold-based lateral flow test is available from INDOOR Biotechnologies, Ltd. Rapid Test for Mite Allergens (RAPID) at http://www.inbio.com/Rapid Test Kit.html

* Allergens with established WHO International reference preparations

Residential Trigger	Assessment Strategy							
	Sampling		Analysis		Test Applicability			
11990	Method	Reliability	Method (units)	Quality assurance	Important Species	Data Obtained ²		
Molds	Dust or surface sampling by vacuum, surface wipe, swab,	ampling by vacuum, urface wipe, swab, tape ulk sampling of pontaminated iaterials ir sampling with atic or personal	ELISA 3 (µg/g or pg/m3)	Not currently reliable for fungi (e.g., Alternaria counts must be very high)	Aspergillus, Alternaria, Cladosporium	Allergen levels (Asp f 1 and Alt a 1)		
	or tape Bulk sampling of		Spore Count	Intact spores may not account for total allergen load	All (Aspergillus and Penicillium species difficult to identify)	Concentration of spores; spore identification		
	contaminated materials Air sampling with static or personal sampler		Culture	Viable fungi may not account for total allergen load	All (may miss poorly competing species of low viability, e.g., Stachybotrys chartarum.)	Species identification; Estimates of fungal concentrations		
			Chemical biomarkers (ergosterol or beta d- glucan)	Good indicators of total biomass; cannot identify species	Not species specific: Components in all fungal hyphae and spores (as well as some algae.	Concentration of chemical biomarker; Estimates of fungal biomass		
					Beta d-glucan is biologically active. Yeasts.			
			Polymerase chain reaction (PCR) based technologies (i.e., genetic probes)	Accurate: Based on targeting species-specific sequences of DNA for the 130 species for which probes have been developed	Species specific, including but not limited to Alternaria, Aspergillus, Cladosporium and Penicillium	Mold identification to the species level		
			Particle immunostaining	Extremely sensitive	Alternaria	Allergen levels		

Table 2. Overview of Assessment Strategy Options for Selected Residential Asthma Triggers ¹ (continued)

¹ See text for references.

² Allergens listed in this column are those for which monoclonal antibodies are typically commercially available for immunoassay purposes(see INDOOR Biotechnologies website, <u>http://www/inbio.com/index.html</u>) ³ Quantitative differences between allergen standards are currently an important source of assay (ELISA) variability.

⁴ Additional information on ACLOTEST® is available on the internet from the Allergy Buyers Club, http://store.yahoo.com/allergybuyersclub/dustmitetestkit.html.

⁵ Additional information on the gold-based lateral flow test is available from INDOOR Biotechnologies, Ltd. Rapid Test for Mite Allergens (RAPID) at

http://www.inbio.com/Rapid Test Kit.html

* Allergens with established WHO International reference preparations

3.1 Environmental Sampling and Analysis

In general, quantitative assessment of indoor allergens involves sampling of a representative environmental medium in the home (most commonly dust or air) and, following extraction, estimation of allergen levels in that sample via direct measurement of the allergen (i.e., immunoassays). Levels of the allergen source material may also be estimated via some other marker, such as by estimating the total fungal biomass from $(1\rightarrow 3)$ β -D-glucan analysis.

Sampling. Indoor environments generally contain large reservoirs of allergens in settled dust accumulated in carpets, bedding, and upholstery. Depending on dust disturbing activity, only a very small amount is usually airborne at a given time (with the exception of cat and other animal allergens, which may also have relatively high airborne levels). The primary route of exposure to allergens is presumed to be inhalation of airborne particles. Reservoir levels are more reflective of an integrated chronic exposure rather than being markers for short-term exposures. Therefore, environmental assessment with regards to allergens has primarily involved measuring allergen levels in dust samples obtained from reservoir sources within the house. Bedroom concentrations are typically used as markers of allergen exposure usually occurs (NAS, 2000).

For allergens associated with dust, it has been suggested that repeated sampling of dust over time gives better information about long-term exposures of the individual to allergens due to temporal variability (Hirsch et al., 1998). In addition, because it has been observed that concentrations of allergens in dust can vary significantly over short distances within a room, by convention, the sample with the highest allergen concentration is typically used as the measure of exposure (O'Meara and Tovey, 2000). Surfaces vary widely in amount of total dust from room to room or home to home. Therefore, when collecting samples of settled dust, it is advisable to record the area sampled in order to report results as the mass of allergen or other agent per unit of area (e.g., m^2) as well as concentration per gram of dust.

Although sampling season has been shown to be a source of variation in cat allergen (possibly associated with fur shedding cycles or the time a pet spends indoors), and mite, fungi, and cockroach allergen levels (due to seasonal changes in temperature and humidity) in household dust, the influence of other home characteristics can far outweigh the significance of seasonal variation (Chew et al., 1999; Flannigan, 1997). For example, Chew et al. (1999) 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, thus far outweighing the seasonal effects observed.

House dust mite and cockroach related allergen particles are typically relatively large in size (10- 25μ m), and as such, tend to remain airborne for comparatively short periods of time (on the order of minutes). Therefore, because there is very little or no airborne dust mite or cockroach allergen in an undisturbed room, air sampling for these allergens is relatively uncommon. The currently accepted method for assessing dust mites and cockroach exposures is to measure (via assay, as discussed below) concentrations of allergens in dust samples collected by vacuuming, preferably

in the bed or bedroom. Sampling locations may vary for cockroach allergens because they are usually found in greater concentrations (e.g., up to an order of magnitude) in kitchens and bathrooms due to the availability of food and water sources. Because cat and dog allergens are carried on smaller airborne particulates that remain suspended in the air for long periods of time, air sampling is often successfully used to assess these allergen levels for intervention studies. Both air and dust sampling are used to estimate environmental levels of fungi.

In summary, the pros and cons of dust vs. air sampling are as follows:

Settled dust sampling:

- Pros: Better indicator of time-integrated exposure. Less temporally variable.
 Better indicator of exposure to house dust mite and cockroach allergens, because particles tend to remain airborne for relatively short time periods.
 Sample collection is relatively fast, easy and inexpensive.
- Cons: May be poor indicator of short-term exposures.

Air sampling:

- Pros: Captures inhalable particles. Better indicator of short-term exposure.
 - Allows fluctuations in exposure to be assessed over a week or a day.
 - Successfully used to assess cat and dog allergens, because particles remain airborne for relatively long time periods.
 - May be useful if it is suspected that ventilation systems are contaminated.
- Cons: -Airborne concentrations for many allergens are generally low, so samples encounter limits of analytical sensitivity.
 - Allergen levels in air vary with amount of disturbance.
 - To represent longer term exposure, a much larger number of samples must be collected.

- May provide poor representation of exposure to house dust mite and cockroach allergens, because particles tend to remain airborne for relatively short time periods.

Sampling of dust reservoirs is achieved using a suction device. HUD has developed a recommended "Vacuum Dust Sample Collection Protocol for Allergens" for use by HUD Healthy Homes Initiative grantees (HUD, 2004a). The protocol is adapted from sampling methods used in the National Survey of Lead in Allergens in Housing and the Inner-City Asthma Study, and it is supported by a companion HUD document, "Background and Justification for a Vacuum Sampling Protocol for Allergens in Household Dust" (HUD, 2004b). These and other reports containing dust sampling methods are available on HUD's website at http://www.hud.gov/offices/lead/hhi/hhiresources.cfm#techresource. A hand-held portable vacuum cleaner, electric powered, not battery operated, is recommended, with a filter, sleeve or

vacuum cleaner, electric powered, not battery operated, is recommended, with a filter, sleeve or thimble dust collection device. Most electric powered canister vacuum cleaners are essentially equivalent for use in indoor dust sampling for allergen analysis, but it is necessary to choose a

model that can accommodate the dust collection device that will be used (HUD, 2004a). Various factors, including design of the vacuum collector, surface characteristics, and other environmental characteristics have all been shown to affect the efficiency of dust collection (Wang et al., 1995; NAS, 2000). For example, Wang et al. (1995) observed that when collecting dust with a vacuum sampler from a shag carpet surface, lower relative humidity (e.g., around 20 percent, as would be encountered during a dry, cold season) increased the intensity of the electrostatic field on the carpet and thus significantly decreased the collection efficiency of the vacuum. Sampling locations vary with the objectives and resources of the study. They commonly include the floor and bedding of the bedroom, the floor and upholstered furniture in the common living area, and the kitchen floor.

For investigations of mold contamination in homes, source sampling methods, including bulk and surface sampling, may also be used. In bulk sampling techniques, portions of environmental materials (e.g., settled dust, sections of wallboard, pieces of duct lining, carpet segments, or return air filters) are collected and tested to determine if molds have colonized a material and are actively growing, and to identify surface areas where previously airborne mold spores and fragments have settled and accumulated (Martyny et al., 1999). Simple surface sampling techniques, accomplished by either pressing a collection material (e.g., a contact plate or adhesive tape) against a surface, or by wiping an area with a wetted swab, cloth, or filter, may also be used in mold contamination investigations (Martyny et al., 1999).

Where appropriate, sampling of airborne particulates is typically performed using devices such as static samplers (placed in a fixed location in the room) and personal breathing zone or nasal air samplers (O'Meara and Tovey, 2000). The most commonly used methods available today for volumetric air sampling are based on one of the following principles: inertial compaction (e.g., multiple-hole impactors, slit samplers), centrifugal collection (e.g., agar-strip impactors, cyclone samplers), filtration (e.g., cassette filters attached to portable pumps), and liquid impingement (e.g., three-stage impingers) (Martyny, 1999). Gravitation or settling techniques (e.g., longer-term collection of settled spores onto a culture plate or microscope slide) can also be used, but due to large temporal and spatial variations, gravity techniques cannot be used as a substitute for volumetric measurements (O'Meara and Tovey, 2000; Martyny, 1999). For mold analysis, air sampling collection times are important. Anderson samplers (multiple-hole impactors) are used for only a few minutes because of effects on the culture plate. Such short sampling times are not a practical reflection of the environmental exposure. Rather longer sampling under usual activity levels (6-72hrs. at 10-20L/min with collection on polycarbonate filters) gives a more representative picture of airborne fungi (Dillon et al., 1999).

Allergen Analysis. For allergen analysis, collected dust samples are typically sieved to separate out the fine dust fraction (i.e., using a 60-mesh metal sieve that allows particles smaller than 250 µm in diameter to pass through), which is then extracted with a buffer solution, serially diluted, and then applied to the appropriate quantitation test. To measure allergen levels, enzyme-linked immunosorbent assays (ELISAs, or also commonly called immunoassays) have been developed for many allergens. Immunoassays are a laboratory technique that makes use of the specific binding between the antigen associated with an allergen and its homologous antibody in order to

identify and quantify a substance in a sample. They generally provide very accurate quantitation (Chapman et al., 2000). However, although immunoassays for numerous allergens have been developed, only relatively few are readily available from commercial laboratories. Those that are typically available include immunoassays for dust mite (Der p 1 and 2, Der f 1 and 2, and Blo t 5), cat (Fel d 1), dog (Can f 1), mouse (Mus m 1), rat urine (Rat n 1), and cockroach (Bla g 1 and 2) allergens (e.g., see Indoor Biotechnologies, Inc. at http://www.inbio.com/index.html). Immunoassays have also been developed for several important indoor mold allergens, including those from *Aspergillus fumigatus*, *Alternaria alternata*, and *Cladosporium herbarum* (Bush and Portnoy, 2001). However, immunoassay technology for molds is not as highly developed or well-standardized as that for house dust mite, animal, or cockroach allergens (Bush and Portnoy, 2001). Only assays for *Alternaria* (Alt a 1) and *Aspergillus* (Asp f 1) are currently widely available (Vailes et al., 2001).

At present, many different immunoassays are being used to measure the same allergens, but comparisons of allergen levels in different studies can be made using standard reference preparations. To date, international reference preparations for allergens have been developed by the World Health Organization (WHO) only for one species of mite (*D. pteronyssinus*) and for dog allergen (Chapman et al., 2000). However, other standards for mite, cat, dog, and cockroach have been developed by numerous research groups and companies and are widely available in the U.S. for 'in-house' or commercial use, although their stability and accuracy has not yet been established (Platts-Mills, et al., 1997). Nevertheless, a recent review of allergen detection and avoidance measures recommends the use of home collection kits as an alternative to professional sampling during home inspections for measuring allergen levels in settled dust (Eggleston, 2003).

Particle immunostaining is a relatively new technique that involves a protein-binding membrane, immunostaining of bound allergens, and examination of stained samples under a microscope where the density of staining is determined using image analysis (O'Meara and Tovey, 2000). This technique has been used in research settings to measure airborne mite (Der p 1 and Der p 2), cockroach (Bla g 1), cat (Fel d 1), dog (Can f 1) and *Alternaria* allergens in undisturbed indoor environments (Poulos et al., 1998, De Lucca et al., 1998, Tovey et al., 1998, and O'Meara et al., 1998, as cited in O'Meara and Tovey, 2000). It is extremely sensitive (on the order of sub picograms of allergen) and appears to have high repeatability in combination with nasal air samples (O'Meara and Tovey, 2000).

Other Methods for Analyzing Mold Levels. Current methods, in addition to immunoassay technologies discussed above, available to analyze environmental samples from the home for mold hazards include:

- Counting cultured colonies by mold species.
- Identifying and counting spores.
- Chemical analysis of fungal components and biochemical/immunochemical markers to quantify total fungal loads (biomass).
- Polymerase chain reaction (PCR) based technologies (i.e., genetic probes) to identify fungal species.

Culture or spore counts of air or dust samples can be used to assess fungal populations; however, because allergenic spores may not be viable (i.e., culturable), the culture method may underestimate true allergenic potential. Also, in cultures containing multiple species (as is often the case) some species may not compete well and may not grow sufficiently for accurate enumeration or even identification. Non-culture methods can also be used to estimate total fungal allergen loads (biomass), although, generally, these methods do not allow for identification of species.

Non-culture methods may be based on chemical components (biomarkers) found in all or some fungal species (e.g., ergosterol in the cell membranes of fungi and extracellular polysaccharides (EPS) produced in mycelial cell walls), and can also include fungal components which have themselves been directly associated with adverse health effects (i.e., β (1 \rightarrow 3)-glucan) (Flannigan, 1997). These methods could prove particularly useful in situations where fungal allergens are not otherwise easily differentiated on the basis of morphology (e.g., *Aspergillus* and *Penicillium*) or where culture methods are not useful because spores have lost their viability (O'Meara and Tovey, 2000). Volatile organic compounds (VOCs) produced by fungi can also be used as markers of fungal growth, and in particular, may be useful for detection of hidden mold growth that has permeated porous walls in buildings (Dillon et al., 1999).

Quantitative polymerase chain reaction (QPCR) based technologies (i.e., genetic probes), unlike other non-culture methods, can be used to identify biological particles, such as fungi, to the species level (Flannigan, 1997). The technology is based on targeting short, species-specific sequences of DNA. EPA's Office of Research and Development, National Exposure Research Laboratory, has recently refined a DNA-based system that allows rapid identification and quantification of molds in a matter of hours. The analytical methods are published at the website: http://www.epa.gov/nerlcwww/moldtech/htm. Beneficial attributes of QPCR are: (1) it is species specific, which may allow assessment for certain mold species known to be associated with health effects or environmental conditions; (2) unlike live culture analysis, it reports non-viable as well as viable molds, which is important because non-viable molds are potentially allergenic; (3) it results in fewer "non-detects" than live culture analysis; (4) it is apparently more reliable than live culture analysis because not all species may grow on the media used and because fast-growing species may overtake the slow-growing species; (5) it finds higher concentrations than culture analysis, sometimes by orders of magnitude; and (6) it is quicker and easier (Vesper et al., 2005; Vesper et al., 2004; Meklin et al., 2004). In recent studies, the cited investigators found that QPCR results did not correlate with culture-analysis results. Also, results of QPCR-analyzed settled-dust samples did not correlate with QPCR-analyzed short-term air samples (five minutes or less); similar results have been reported based on viable count methods. Current disadvantages of OPCR include the facts that DNA probes have been developed for only 130 fungal species, and the relatively high cost.

Using mold specific QPCR, the investigators cited in the previous paragraph found that certain molds, which they labeled Group I molds, are found in higher concentrations in water-damaged homes than in other homes, while other molds (labeled Group II molds) are found in all homes

(Vesper et al., 2004). One way this information may be useful is in identifying homes that have suffered water damage but do not display easily identifiable signs of water damage. Another may be in narrowing the list of molds for which QPCR analysis is necessary. Also, the investigators compared QPCR-analyzed dust sample results from water-damaged homes of asthmatic children with those from control-group homes and found (1) that only Group I molds had higher concentrations in the water-damaged, asthmatic-occupied homes compared to the control homes, and (2) that certain Group I mold species had significantly higher concentrations. The authors conclude, "If Group I molds are discovered, water-damaged remediation and mold removal might be considered as part of the total prevention plan in an asthmatic child's home."

3.2 <u>New Techniques for Home Testing</u>

Immunoassays are generally time-consuming and require specialized laboratories. Recently however, as the importance of indoor allergen avoidance and the need for simple, rapid, dust sampling and allergen testing has become apparent, several office or home-based testing technologies have been developed. A few simple test kits that use monoclonal antibody (MAb)based technology (the technology used in home pregnancy tests) are currently available. These technologies use antigen-specific antibodies which are attached to membranes (as dipsticks or cassettes) to bind proteins present in a sample (in this case, allergens present in an extracted and diluted sample). In the final step of the test, a second allergen specific antibody that has an additional molecule linked to it, such as an enzyme that changes the color, is then added. If a specific allergen is present, the intensity of the color that is produced is in proportion to the allergen concentration. In the absence of the allergen, the second purified antibody will not be bound and no change in sample color will occur. For allergen screening of indoor samples, these types of tests usually only provide a result above or below a threshold value (O'Meara and Tovey, 2000). Some of these tests can detect multiple allergens using one dust sample, such as a commercial method called DUSTSCREEN® (CMG-HESKA, Fribourg, Switzerland) which can detect D. pteronyssinus and D. farinae mite allergen, Felis domesticus (cat) allergen, and Blatella germanica (cockroach) allergen (Chapman et al., 2000; DeWeck et al., 1998 as cited in Chapman et al., 2000). Two types of quick tests have also been developed specifically for dust mites, including the ACLOTEST® and the gold-based lateral flow quick test (Chapman et al., 2000). The gold-based lateral flow test (Rapid Test for Mite Allergens (RAPID®)) is sensitive to a detection limit of approximately 100 pg, detects both D. pteronyssinus and D. farinae, and produces results within 10 minutes (INDOOR Biotechnologies, Ltd. at http://www.inbio.com/Rapid Test Kit.html) (Chapman et al., 2000; Tsay et al., 1999). The ACLOTEST® (Lofarma, Milan, Italy) detects D. pteronyssinus and D. farinae mite allergens (including Der p1 and Der f1) and is sensitive to 0.5 µg/g dust (Pure n Natural Systems, Inc., http://shop.store.yahoo.com/purennatural/00-dmtk.html) (Mistrello et al., 1998 as cited in Chapman et al., 2000). A home dust collection device called the MITEST® collector has also been recently developed, and consists of a collector that fits on the end of a tube wand vacuum (INDOOR Biotechnologies, Ltd. at http://www.inbio.com/Mitest Dust Collector.html). After vacuuming for 2 minutes, the collector is capped, shaken with an extraction solution for 5 minutes, and then applied to the allergen test. Using this collector together with the RAPID®

gold-based lateral flow test, a dust sample can be collected, extracted, and tested within 15 to 20 minutes (Chapman et al., 2000).

3.3 Interpretation of Results

The challenge in interpreting results from either visual assessment and occupant surveys or from environmental sampling is twofold: first, determining the degree to which the results indicate potential for human exposure and subsequent health effects, and second, determining the relative severity of different individual hazards. An extensive discussion of the factors associated with exposure and risk for asthma associated with residential exposures is beyond the scope of this paper. However, some representative issues associated with interpretation of results include:

- The primary route of exposure to allergens is presumed to be inhalation of airborne • particles, and thus reservoir levels are not good markers for short-term exposures. For example, due to activity and resulting dust disturbance in a home, studies have found large variations in the amount of a specific allergen that is airborne at a given time, often with a 50-fold difference in the concentrations of airborne allergens detected in homes within one experiment (O'Meara and Tovey, 2000). Another limitation of assessing exposure via the concentration of allergen per gram of settled dust is that it inadequately characterizes the total allergen burden in a house, due to differences in amounts of total dust (NAS, 2000). The correlation between airborne and dust reservoir allergen levels has not been well studied, but some data suggest that reservoir dust concentrations are poor predictors of airborne levels (O'Meara and Tovey, 2000). These investigators further suggest that this may be, in part, due to the fact that reservoir levels are usually expressed as concentrations (μ g allergen per gram of dust). Expressing reservoir levels as surface loadings (μ g per m²) may be a more appropriate measure of reservoir allergen for purposes of predicting airborne levels (Takaro et al., 2004). In general, however, the measurement of allergen concentrations in dust is currently more feasible and consistent than air sampling, and it is therefore more typically employed.
- Regarding pet allergens, Platts-Mills et al. (1997) suggested that cat allergen concentrations in reservoir dust might not adequately characterize inhalation exposure. However, for the purposes of low-cost health assessment in a residential setting, environmental sampling would not be necessary where the presence of a pet, and thus pet allergen, is known or can be imputed.

In general, there is significant variability in sample results dependent on the time and location of sampling and significant uncertainty concerning the relationship between environmental samples and exposure. There is also considerable variability associated with the determination of allergen-specific concentrations in dust samples using ELISA. HUD initiated a study in which commercial, academic, and municipal laboratories were provided with dust samples from the same batches of reference dust to analyze for up to six allergens (Pate et al., 2005). Coefficients of variation on the estimated geometric mean allergen concentrations ranged from 61% - 93%, and in most cases between-laboratory variability in analytical results was significantly greater than

within-laboratory variability. The results indicated that analytical results could generally be used to determine if allergen-specific concentrations exceeded thresholds of interest with reasonable certainty; however, they also supported the importance of improving the standardization of laboratory procedures for processing and analyzing samples for allergens using ELISA methods. The results also supported the value of incorporating quality control dust samples into the sample stream to assess laboratory performance when conducting research and evaluation activities.

Other important issues related to the interpretation of environmental samples remain, and many of these are topics for future research as mentioned below in Section 5.

Guidelines for Comparison. Table 3, below, presents estimated threshold levels that have been proposed or suggested for common indoor allergens, against which allergen levels in the home may be compared to determine the level of potential hazard. The table provides threshold levels for allergic sensitization and for asthma symptoms, i.e., the level representing a risk of sensitization to the allergen and the level at which most allergic patients will experience symptoms. Except for dust mites, these threshold levels are not well established.

	Threshold Level				
Allergen	Allergic Asthma Sensitization Symptoms		Typical Sample Characteristics		
Dust mite allergen (Der f 1 + 2 µg/g ^a 10 µg/g ^a Der p 1)		10 μg/g ^a	Collection: Dust, by vacuuming (bed and bedroom) Analysis: Assay group 1 allergens (μ g/g) or dust mite count		
Cockroach allergen (Bla g 1) 2 Units/g ^b 8 Units/g ^b		8 Units/g ^b	Collection: Dust, by vacuuming (bedroom, kitchen, bathroom); trapping Analysis: Assay of allergens (Units/g) or cockroach identification and counts		
Cat (Fel d 1)	1 µg/g °	8.0 µg/g ^c	Collection: Dust, by vacuuming (living room floor and furniture); air sampling Analysis: Assay of allergens (μ g/g)		
Dog (Can f 1)	2 µg/g °	10 µg/g °	Collection: Dust, by vacuuming (living room floor and furniture); air sampling Analysis: Assay of allergens (μ g/g)		
Mouse (Mus m 1)	1.6 µg/g ^c		Collection: Dust, by vacuuming (whole house); air sampling Analysis: Assay of allergens (μ g/g)		
Fungal allergen	No allergen specific thresholds ^d		Collection: Air sampling; surface sampling Analysis: Spore counts, culturable fungi, total biomass/biomarker		

 Table 3. Current Threshold Levels for Assessing Common Residential Allergens

^a Platts-Mills et al., 1995

^b Eggleston and Arruda, 2001

^c Cat and dog threshold levels used by Ingram et al. (1995) and Custovic et al. (1998b). Mouse levels based on Phipatanakul et al. (2000b).

^d Bush and Portnoy (2001) suggest that indoor spore counts equal to or greater than 1000/m³ and colony counts on the order of 1000 to 10,000 CFU per m³ likely represent indoor fungal contamination. Portnoy et al. (2005) concluded that "total airborne spore counts attributable to indoor sources greater than 1,000 spores/m³ indicate a concern and those greater than 10,000 spores/m³ indicate a definite problem." Other suggested guidelines for the upper limit for airborne fungi in non-contaminated indoor environments reported in the literature range from less than 100 colony forming units (CFU) per m³ to greater than 1000 CFU per m³ (Rao et al., 1996). Established threshold levels for mold genera do not exist at this time (Jacob et al., 2002).

4.0 METHODS BEING USED TO MITIGATE ASTHMA TRIGGERS IN THE HOME

For many allergens, integrated, or multi-faceted approaches for indoor environmental interventions are considered most effective. Two primary components of an integrated approach are:

- 1. Removal or cleaning of allergen reservoirs.
- 2. Control of new sources of exposure.

Chapman et al. (2000) reported that a review of research generally suggested that a reduction in allergen levels in key reservoirs (bedrooms, living rooms, and basements) by more than 50% could reduce the risk of asthma development and severity. However, the authors also noted that even if removal of new sources reduces allergen exposure by up to 80% or 90%, allergen levels in reservoirs in homes with very high allergen levels (e.g., >10 μ g/g for mite allergens) may still remain higher than the proposed threshold levels for sensitization (e.g., 2 μ g/g for mite allergens). Platts-Mills et al. (1997) suggested that, where possible, mitigation protocols should be evaluated using measurements of both reservoir dust concentration and quantity together with airborne levels during disturbance.

Table 4 summarizes five recent multifaceted interventions in the homes of asthmatic children. The Inner City Asthma Study enrolled 937 children, aged 5-11, with asthma, living in generally lower income neighborhoods in the Bronx, NY; Boston, MA; Chicago, IL; Dallas, TX; New York, NY; the Seattle and Tacoma, WA, area; and Tucson, AZ. It focused on reducing exposure to dust mites, passive smoking, cockroaches, pets, rodents, and mold. Interventions were tailored to the allergic sensitivities of each child and environmental exposures observed in the home. After two years, children in the intervention group had significantly fewer days with symptoms than those in the control group, and their homes had greater declines in allergens. Reductions in the levels of cockroach allergen and dust-mite allergen on the bedroom floor were significantly correlated with reduced complications of asthma (Morgan et al., 2004; Gruchalla et al., 2005). Kattan et al. (2005) reported that the intervention used in the Inner City Asthma Study cost \$1,469 per family and that over the year of intervention and a year of follow-up, the cost was \$27.57 per additional symptom-free day (95% confidence interval, \$7.46-\$67.42). The authors concluded that the intervention was cost-effective.

Another study, in the Seattle-King County, area used an approach similar to that in the Inner City Asthma Study. Home asthma triggers were reduced, caregiver quality-of-life improved, and asthma-related urgent health services declined due to the intervention. Asthma symptom days declined significantly in both the high-intensity and the low-intensity (or control) groups, but the effect due to the intervention did not reach statistical significance in this measure (Krieger et al., 2005; Takaro et al., 2004; Krieger et al., 2002). Two differences between this Seattle study and the Inner City Asthma Study (ICAS) are: (1) the Seattle study did not provide HEPA air purifiers whereas the ICAS did if the child was exposed to passive smoking, sensitized and exposed to cat

or dog allergens, or sensitized to mold; and (2) home visits in the Seattle study were made by community health workers, whereas the ICAS used research assistants. Both studies emphasized educating and equipping caregivers for environmental remediation, but the Seattle study may have given greater emphasis to providing support to the caregiver in other difficult aspects of life.

A similar study in Denver reported less successful results, although these findings are considered preliminary (Klinnert et al., 2005). In this study, the enrolled children were aged 9 to 24 months, whereas the ICAS and Seattle studies enrolled children aged 5-11 and 4-12 years, respectively. Vacuum cleaners were provided, but not HEPA air purifiers. Nurse home visitors provided caregivers with education on respiratory illness management and continual support for mental health. At 12 months, the study was effective in reducing several environmental exposures and improving illness management, but it failed to reduce respiratory symptoms or medical use in the intervention group relative to the control group.

Study	Study Cohort	Interventions	Results
Inner City Asthma Study (a)	937 asthmatic children, aged 5- 11, living in low- income neighborhoods of 7 American cities	Individualized actions tailored to children's sensitivities and exposures in home. Major effort to educate and equip caregivers in environmental remediation. Bedding encased. HEPA vacuum provided. Air purifier provided for ETS, pet allergens, & mold. Pest extermination for cockroaches. Research assistants made a median of 5 visits to intervention-group homes over a 12-month period.	Intervention group had fewer symptom days and greater declines in allergen levels than control group. Reductions in cockroach and dust-mite allergens were correlated with reduced asthma morbidity. Cockroach allergens appeared to have a greater effect on asthma morbidity than dust mites or pet allergens in inner city children. Intervention group had significant reductions in the disruption of caregivers' plans, caregivers' and children's lost sleep, and school days missed. Cockroach exposure and sensitivity predominated in northeastern cities; dust mite exposure and sensitivity were greater in the south and northeast.
Seattle-King County Healthy Homes Project (b)	274 low-income households with asthmatic children aged 4-12	Individualized actions. Major effort to educate and equip caregivers in environmental hazard reduction, and to support them in dealing with difficulties of life. Bedding encasements provided. Low-emission vacuum provided. Door mats and cleaning kits provided. Roach bait and rodent traps provided. Community health workers made 5-9 visits to high- intensity intervention homes over a 12-month period.	The high-intensity intervention group improved significantly more than the low-intensity group in urgent health services use and in caregiver quality-of-life index. Asthma symptom days declined more in the high-intensity group, but not statistically significant. The high-intensity group had a decrease in the asthma trigger composite score that was significantly greater than that for the low-intensity group. Improvements in mean scores for condensation, roaches, moisture, and dust weight were significant for the high- intensity group but not for the low-intensity group.
Childhood Asthma Prevention Study, metropolitan Denver (c)	181 wheezing infants, aged 9 to 24 months, from low-income families	Individualized actions. Major effort to educate and equip caregivers in environmental hazard reduction and symptom recognition and management, and to support them in dealing with difficulties of life. Smoking in child's presence was discouraged. If cockroach allergen levels were greater than 2 U/g, cleaning materials and traps were provided, and advice was given on removal of food sources. Pet removal and cleaning recommended if dog and cat dander were elevated. Vacuum cleaners were provided. Nurses with community outreach experience made a median of 15 visits or phone calls per home during a 12- month period.	These results are considered preliminary: At 12 months, cockroach allergen levels were significantly reduced in the intervention group. The intervention group had greater reductions in dog dander than the control group, but the difference was not significant. The difference in cat dander change was not significant. Among infants with detectable urinary continine, levels were significantly reduced in the intervention group. Intervention-group caregivers had significantly greater improvement in asthma knowledge and medical provider collaboration. Neither respiratory symptoms nor emergency department visits or hospitalizations showed positive intervention effects.

Table 4. Summary of Recent Multi-faceted Environmental Intervention Studies

Study	Study Cohort	Interventions	Results
Study of effects of home moisture remediation on asthma morbidity, metropolitan Cleveland (d)	62 asthmatic children, aged 2 to 17 years, living in homes with indoor mold.	All participants received medical and behavioral information and support. Remediation-group homes received construction repairs focused on reducing water infiltration, removal of water- damaged materials, HVAC alterations, and environmental cleaning. The mean cost of remediation was \$3,458.	Results after one year were: Remediation-group subjects had fewer symptom days than control-group children, and the difference was significant when adjusted for baseline asthma severity and season. Remediation group children had significantly fewer acute care visits. Reductions in endotoxins were greater in the remediation group, as were reductions in mold scores. Allergen concentrations for dust mite, cockroach, and rodent did not decline significantly.
Community-based participatory study of effects of environmental interventions on asthmatic children in Boston public housing (e)	50 asthmatic children in Boston public housing.	Asthma education for caregivers and limited case management. Provision of new mattress with microfiber technology. Integrated pest management (IPM). Industrial cleaning. Sealing of possible pest penetrations. Education of residents about IPM and provision of tools for reducing clutter and pest access to food.	No control group. Respiratory symptoms improved significantly. With logistic regression, the following variables were predictors of improvements in respiratory health: number of allergens with high concentration reductions, reductions in cockroach allergen levels, and improvements in neighborhood social cohesion or individual social support.

Table 4. Summary of Recent Multi-faceted Environmental Intervention Studies, continued

Sources:

(a) Morgan et al., 2004; Gruchalla et al., 2005(b) Krieger et al., 2005; Takaro et al., 2004; Krieger et al., 2002

(c) Klinnert et al., 2005

(d) Kercsmar et al., 2005

(e) Levy et al., 2005

In the Cleveland area, researchers took an approach that was different from the three studies described above (Kercsmar et al., 2005). While all 62 participants received medical and behavioral intervention, the remediation group received construction repairs focused on reducing water infiltration, removal of water-damaged building materials, HVAC alterations, lead hazard reduction, and environmental cleaning. Households with no visible mold were excluded from the study. Examples of intervention work include cleaning mold from hard surfaces, removing mold exposure pathways, stopping rainwater intrusion, exhausting water vapor from kitchen and baths, repairing plumbing leaks, repairing a faulty cold-air return, disconnecting and redirecting downspouts, and reducing moisture in crawlspaces and basements. The mean cost of remediation was \$3,458. Subjects in the remediation group had fewer symptom days than those in the control group, but the difference was not statistically significant. However, when adjusted for baseline asthma severity and season, the difference was significant. Children in the remediation group had significantly fewer acute care visits than those in the control group. Reductions in endotoxin concentrations were greater for the remediation group, as were reductions in mold scores. Allergen concentrations for dust mite, cockroach, and rodent did not decline significantly.

Researchers in Boston measured the effects of a community-based multi-faceted approach in homes of 50 asthmatic children in public housing (Levy et al.;2005). Although this study lacked a control group, it did find, with logistic regression, that the following variables were among the most significant predictors of improvements in respiratory health: the number of allergens with high concentration reductions, reductions in cockroach allergen levels, and improvements in neighborhood social cohesion or individual social support. The authors point out that, "significant reductions in symptoms among those who had improved perceptions about their neighborhood, who had improved social support, and who had enough reduced fear of violence to allow their children to play outside, may indicate that the social connections made during the study had a direct or indirect health benefit."

An overview of common mitigation methods and their relationship with multiple asthma triggers in the home is presented in Table 5.

Selected methods of mitigating asthma triggers in the indoor environment are described below. While the following discussion is structured by type of allergen, the reader should bear in mind that the major studies described above indicate that an integrated approach that addresses all the identified sensitivities of a subject seems to have the best chance of effectiveness. Most patients with asthma are sensitive to and exposed to multiple allergens. Also, as research suggests that children and lower-income inner city residents are particularly vulnerable populations for asthma sensitization, frank morbidity, and mortality, much mitigation research has focused on finding ways to mitigate asthma triggers for these populations.

	Asthma Triggers Potentially Affected ²					
Mitigation Method	Dust mites	Cockroaches	Pets and Rodents	Molds	Chemical Agents	
Moisture control	\checkmark	\checkmark				
Ventilation			\checkmark	\checkmark	\checkmark	
Cleaning	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark	
Air filtration			\checkmark	\checkmark		
Minimization and/or replacement of soft interior furnishings ³	\checkmark	\checkmark	\checkmark	\checkmark		
Encasement of mattresses and pillows		\checkmark	\checkmark			
Behavior modification		\checkmark	\checkmark	\checkmark	\checkmark	

Table 5. Major Mitigation Methods and Asthma Triggers Potentially Affected ¹

¹ See below for additional discussion of each mitigation technique

² Only selected triggers are listed

³ Soft interior furnishings might include items such as carpeting and upholstered furniture

4.1 <u>Dust Mite Allergens</u>

Common intervention methods reported in the literature for residential mitigation of dust mite allergens include:

- Maintaining a relative indoor humidity less than 50%.
- Encasement of mattresses and pillows in covers (<10 µm in pore size) and washing of bedding in hot (>130°F) water.
- Removal of fitted carpets (especially in humid zones).
- Replacement with non-VOC containing flooring (e.g., Marmoleum).
- Dry vacuuming and dry steam cleaning (carpets, floors, and upholstered furniture).
- Removal or cleaning of upholstered furnishings and drapes.
- Removal of soft toys for children, or periodically (e.g., monthly) freezing them.
- Regular year-round cleaning protocol.

Evidence generally supports the effectiveness of the use of a combination of physical measures reducing mite allergen exposure and severity of asthma symptoms (NAS, 2000). Strategies to control mite growth may vary according to the type of indoor environment and the prevailing climate. For example, in humid climates, maintaining a relative humidity of less than 50% requires tight housing and air conditioning. In areas with seasonal variation in humidity, opening windows for one hour a day during the dry seasons is sufficient to reduce humidity (NAS, 2000). In continually dry areas such as the mountain states and the Southwest, mite growth in houses is

unusual. Additional strategies for moisture control are discussed below in Section 4.4, Mold and Moisture.

The use of impermeable bedding covers, combined with frequent washing of bedding materials, generally has been shown to be effective in reducing house dust mite allergen levels in the bed (Voita et al., 2001; Vaughan et al., 1999a; Mihrshahi et al., 2003). The most effective coverings for bedding have been shown to be permeable to air and water vapor, but tightly woven and impermeable to mites. In a study that tested the effectiveness of different "allergen proof" bedding encasement materials (Vaughan et al., 1999a), tightly woven fabrics (e.g., Pristine from Allergy Control Products, Inc. and Microfiber from Priorities, Inc.) with an estimated pore size of 10 um or less were found to be effective at blocking mite allergen particles. To block the smaller particles of cat allergens, fabrics needed to have a pore size of 6µm or less (Vaughan et al., 1999a). In addition, these tightly woven fabrics only reduced airflow slightly, and thus would not promote moisture buildup in the bedding or cause discomfort sometimes felt with vinyl covers due to heat build-up. Several other specially designed synthetic materials (Softek from National Allergy Supply, Medibed from Comtrad Industries, and Wondertex from GSI) also were observed to effectively block allergen while still allowing for significant airflow. The vinyl covers and materials marketed as "vapor permeable" (Acb Elite from Allergy Control Products, Inc. and Satin Soft from National Allergy Supply) showed significant reductions in airflow. In general, the durability and effectiveness of these encasement materials in situations where frequent washing is occurring is also a factor that should be considered. One tightly woven fabric (Pristine) was tested by washing the material 22 times before testing, and showed very little change in performance (Vaughan et al., 1999a).

Recent evidence suggests that the use of encasement materials may be more effective in preventing allergen exposure among children than it is among adults. Woodcock et al. (2003) found that allergen-impermeable bed covers were ineffective as the sole method of dust mite allergen avoidance in adults, contradicting the findings in numerous studies on children. These results indicate that early intervention (i.e., during childhood) may be crucial to obtaining long-lasting effects through allergen removal (Woodcock et al., 2003).

Studies have shown that physical and chemical interventions can also be effective in reducing dust mite allergen levels in homes. The use of acaricides to kill mites and use of tannic acid to break down allergens, each use followed by cleaning, may be effective in reducing mite allergen levels for short times (i.e., reductions have been observed to last up to a few months) (Vaughan and Platts-Mills, 2000). Therefore, chemical treatments may require frequent re-application (Vaughan and Platts-Mills, 2000). The effectiveness of physical interventions, including intensive vacuuming and dry steam cleaning plus vacuuming, was recently evaluated by Vojta et al. (2001). (In dry steam cleaning in that the surface is said to be completely dry within 15 minutes after application and the carpet backing remains dry throughout the procedure.) Results of treatments showed 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). They also observed that intensive

Version 3

March 2006

vacuuming and steam cleaning resulted in modest reductions in mite levels in upholstered furniture. Based on the observed reductions, the authors concluded that these physical interventions offer practical, effective means of reducing house dust mite allergen levels in lowincome home environments, although long-term control would likely include frequent repetition of the vacuuming and dry steam cleaning treatments (Vojta et al., 2001). Krieger et al. (2002) reported improved effectiveness of vacuuming by study participants when they used power-head HEPA vacuums with a "dirt detector" that indicated when nearly all the dust was removed. Such vacuums are available commercially.

Vacuum cleaners used in allergen cleaning are recommended to have high efficiency particulate air (HEPA) or electrostatic filtration systems on the exhaust air (Platts-Mills et al., 1997; Vaughan et al., 1999b). However, not all such vacuums have the same collection efficiency. Vaughan et al. (1999b) found that although the majority of vacuum cleaners and vacuum cleaner bags specially designed for allergic patients assessed in their study reduced allergen leakage, there was still room for improvement. In general, most of the two- and three-layer microfiltration bags recommended for allergic patients performed well compared to traditional single-layer bags. However, large ranges in performance of the 2-layer bags highlighted variability found between manufacturers.

Air cleaning methods such as HEPA air filtration are more likely to be effective for allergens associated with smaller particles (e.g., cat allergens), because they tend to remain airborne longer than those associated with larger particulates (e.g., dust mite or cockroach allergens) (Chapman, 1998).

4.2 <u>Cockroach Allergens</u>

Common intervention methods reported in the literature for residential mitigation of cockroach allergens include:

- Regular year-round cleaning protocol and limiting open food-stuffs (e.g., enclosing food in plastic containers).
- Eliminating water sources (leaky pipes/faucets, pet water bowls, etc.).
- Safe (targeted) insecticide use and/or extermination.
- Sealing holes and cracks in the home.
- Encasement of mattresses and pillow in covers and washing of bedding in hot (>130°F) water.
- Dry vacuuming and dry steam cleaning (carpets, upholstered furniture).
- Removal of fitted carpets.

The most effective type of cockroach control typically includes using several of these methods concurrently to reduce cockroach populations (Ogg et al., 1994). This multiple tactics approach, which can be applied to any pest population, is called Integrated Pest Management (IPM). For residential cockroach control, an IPM approach should include monitoring suspected infestation areas before and after treatments (e.g., using sticky traps). The primary features of an IPM program for cockroaches include: removal of food, water, and harborages, in combination with

careful placement of the least toxic baits and insecticides necessary (Ogg et al., 1994). Recommended treatments include: implementing structural improvements (such as plugging major holes around plumbing, sealing cracks and crevices to prevent entry and limit hiding places), and improved housekeeping/use of good sanitation practices (i.e., to eliminate food and water resources) (CMHC, 1998; Ogg et al., 1994). Following initial intervention, IPM approaches emphasize continued monitoring in the same areas to assess the success of the control program and whether additional intervention is necessary (Ogg et al., 1994).

Insecticides, including inorganic compounds (e.g., boric acid), pyrethrins, avermectins/abamectin (e.g., Raid®, Combat®), and newer compounds (e.g., fipronil, hydramethylnon, and sulfluramid) are often used in the home to kill cockroaches (Katial, 2003; Vaughan and Platts-Mills, 2000; Eggleston and Arruda, 2001). Boric acid and a less processed form (disodium octoborate tetrahydrate) may be appropriate for persons who are chemically sensitive, and its low mammalian toxicity is consistent with IPM philosophy (Katial, 2003; Vaughan and Platts-Mills, 2000). Studies reviewed by Eggleston (2000) indicated that pesticides can be effective in reducing cockroach populations by as much as 90% for as long as three months. Although these pesticides may be applied in almost any form, gel forms of many roach insecticides are available and can be applied to cracks and other critical areas in a manner that will reduce potential exposures to pets and children (Eggleston and Arruda, 2001). Gels may also be preferred because they have a longer duration of effectiveness and because the insecticides can be carried back to areas of heavy infestation (Katial, 2003). Bait traps that limit access to the pesticide have also been developed (Eggleston and Arruda, 2001) but may require frequent replacement to provide long-term benefit (Katial, 2003).

Preliminary research has indicated that IPM techniques can be effective for cockroach control (Frantz, et al., 1999; Campbell et al., 1999). IPM approaches emphasize the use of "least toxic" pesticides only as needed and confining the area of pesticide application (e.g., with targeted gels, baits, and powders) to reduce the probability of human exposure (Campbell et al., 1999; CMHC, 1998). Results of a study which assessed the effectiveness of a pilot IPM program in controlling cockroaches in an apartment complex, without pesticide sprays, showed that education can influence building residents to accept and comply with an IPM program, and that the program can be effective in controlling cockroaches (Campbell et al., 1999). Another successful urban IPM program credited its effectiveness to strong community involvement at each stage of the project, comprehensive guidance and education by experts, and the cooperation of building managers and others responsible for providing support services to apartments (Brenner et al., 2003). Professional cleaning (as opposed to resident cleaning) has been shown to greatly enhance the effectiveness of IPM approaches, based on the results of a three-pronged intervention to reduce cockroach allergen levels in infested urban homes through resident education, professional cleaning, and insecticide bait placement (Arbes et al., 2003b). In a follow-up study of homes that participated in this six-month intervention, Arbes et al. (2004) found that reductions in cockroach allergen concentrations could be maintained through 12 months with the continued application of insecticide bait alone. IPM can lead to greater sustainability in keeping cockroach populations down, in contrast to extermination only, which typically needs to be repeated.

IPM is likely to have a higher initial cost than more traditional methods, according to two recent studies conducted in public housing. Wang and Bennett (2006) reported that the median costs per apartment during a 29-week period were \$65 for IPM and \$35 for bait treatment. They expected, however, that over the long term IPM would continue to provide better control at a similar cost compared with bait treatment. Miller and Meek (2004) reported that the average cost per apartment of IPM was \$14.60 in the first month compared to \$2.75 per unit for a more traditional treatment of baseboards and cracks and crevices with spray and dust formulation insecticides, but that after four months the costs of the two treatments were no longer significantly different because many of the IPM apartments were shifted to a quarterly treatment schedule. For an entire year, the average per unit cost of IPM was \$4.06 per month compared to \$1.50 for the traditional treatment, which was much less effective (as measured by cockroach-trap catches).

Regardless of the level of reliance on insecticides for controlling cockroach populations, thorough household cleaning is essential for successful cockroach allergen removal (Eggleston and Arruda, 2001). The cockroach allergen (*Blatella germanica*) Bla g 1 is extremely stable; therefore allergens not removed by cleaning may remain indefinitely (Vaughan and Platts-Mills, 2000). It is recommended that general cleaning to remove any food sources be conducted before insecticide application, and that the entire house be intensively cleaned about a week following extermination, including vacuuming, scrubbing walls, floors, countertops and other hard surfaces with water and detergent, and washing bedding, curtains, and clothing, (Eggleston and Arruda, 2001). The effectiveness of different methods of cleaning following extermination has not been well tested; however, vacuum cleaning and tannic acid (to break down allergens) applications have been effective in experimental settings (Eggleston, 2000). Use of a bleach solution (sodium hypochlorite) when cleaning does not seem to improve allergen reduction (Wood et al., 2001). Cockroach allergens located in areas that are not easily accessible (e.g., between cabinets and walls) often cannot be reduced by traditional cleaning techniques.

Interventions requiring carpet removal and replacement with smooth flooring have been shown to be effective in cockroach allergen mitigation, although this method may be impossible in rental units where tenants do not have control of the flooring. Overall, because cleaning and extermination (use of acaricides) effectiveness has been supported for dust mite control, these methods are generally recommended also for cockroach allergens (NAS, 2000).

Until recently, researchers had not demonstrated that reductions in cockroach allergens resulted in reductions in asthmatic symptoms. The Inner City Asthma Study, however, found a significant correlation between cockroach allergen reduction and a decrease in asthma-related morbidity (Morgan, 2004). Basic issues in effective cockroach allergen abatement are (1) the difficulty in reducing allergen levels below suggested thresholds of concern, which are 2 Units/g for sensitization and 8 Units/g for exacerbation, and (2) the difficulty in maintaining low allergen levels over the long term. Suggested reasons for limited effectiveness include: the presence of residual cockroach allergens (due to carcasses remaining in areas that are not easily accessible or lack of thorough cleaning following extermination) and re-infestation problems (especially in multi-family dwellings). As part of the National Cooperative Inner-City Asthma Study (NCICAS), controlled clinical home intervention trials were conducted in 265 homes where children were sensitized to cockroach allergen. Interventions included mattress and pillow

coverings, professional pest control, provision of cleaning supplies, and education on further cockroach allergen removal. Although cockroach allergen levels were temporarily reduced, levels were still well above those reported to cause respiratory symptoms in asthmatics (i.e., >8 Units/g) (Gergen et al., 1999). The authors of the study concluded that cockroach allergens are not easily removed from inner-city homes, especially in multifamily units, and will require further study of cockroach ecology, pest control techniques, and follow-up cleaning methods to allow for successful remediation of cockroach infested houses (Gergen et al., 1999; Eggleston, 2000). In addition, this research emphasizes the importance of addressing multi-family dwellings as a whole, rather than as individual apartments (Gergen, pers. comm.). Wood et al. (2001) also reported that although cockroach allergen levels can be reduced by 80% to 90%, many homes may still have allergen levels exceeding the proposed threshold of 8.0 U/g of dust. In a study of thirteen homes in inner-city Baltimore, Maryland, Eggleston et al. (1999b) found that although cockroach allergen over eight months.

4.3 <u>Pet and Rodent Allergens</u>

Common intervention methods reported in the literature for residential mitigation of pet allergens include:

- Removal of the pet from the home.
- Removal of fitted carpets and upholstery.
- Dry vacuuming and a regular cleaning protocol.
- HEPA air filtration.
- Encasement of mattresses and pillows in covers (<6µm in size).
- Frequent pet washing.
- Use of topical sprays on pets.

Although observed effective in some cases, the extent to which the mitigation measures listed above can control pet allergens is inconclusive (Platts-Mills et al., 1997; NAS, 2000; Chapman and Wood, 2001). Reductions achieved via pet washing and other pet applications have generally been observed to be temporary or insignificant (NAS, 2000). High-efficiency particulate or electrostatic air cleaners are often recommended, especially in bedrooms, although studies on their effectiveness have yielded conflicting results (Chapman and Wood, 2001). For example, van der Heide et al. (1999) observed that the use of air cleaners in bedrooms and living rooms resulted in significant improvements in respiratory symptoms of asthmatic children sensitized to pet allergens, while Wood et al. (1998) found that although HEPA air cleaners reduced airborne allergen levels, no significant improvements in respiratory symptoms occurred. Thus, although airborne levels may be temporarily reduced, reservoirs of pet allergens (e.g., in floor dust) may affect the ability of air cleaners to effectively improve symptoms.

Even following pet removal, research has shown that pet allergen levels may remain elevated for substantial periods of time (NAS, 2000). For example, following cat removal, levels of cat allergen in settled dust may take four to six months to return to levels normally seen in houses without cats, although levels may fall much more quickly if carpets, upholstered furniture and

other reservoirs in the home are removed (Chapman and Wood, 2001). Therefore, additional measures that address reservoir sources (e.g., intensive cleaning of furnishings, beds) are typically required (NAS, 2000).

Airborne cat and other allergen levels may be increased during vacuuming due to disturbance of the dust with the vacuum beater bar and the passage of the allergens through the vacuum cleaner bag into the air (Vaughan and Platts-Mills, 2000). As mentioned above, HEPA or electrostatic filtration systems on the exhaust air of vacuum cleaners are recommended (Platts-Mills et al., 1997). In a study which tested the effectiveness of vacuum cleaners (with special filters) recommended for allergic patients, it was found that new vacuum designs, which use filters before and after exhaust fans along with high quality microfiltration bags, reduced airborne cat allergen levels relative to older vacuum cleaner models (Vaughan et al., 1999b). Three layer bags were required to prevent allergen leakage reliably.

Complicating the determination of appropriate mitigation measures, recent evidence suggests children living in homes with high cat allergen levels (Fel d $1 > 20 \ \mu g$ per gram of dust) might be less likely to become allergic to cats than those in homes with moderate levels (4-20 μg per gram), thus raising questions about the advantages of pet removal in situations where other factors (e.g., neighborhood pets) may keep allergen levels moderately high (Platts-Mills et al., 2000).

High mouse allergen levels have been correlated with cockroach infestation (Phipatanakul et al., 2000a), and both types of pests have similar environmental requirements (e.g., a means of access to the home, food, water). Integrated pest management approaches discussed above for cockroaches can also be effective for controlling rodent populations (Frantz et al., 1999). Phipatanakul et al. (2004) were successful in significantly reducing mouse allergen in 12 intervention homes compared with 6 control group homes in inner-city Boston using an intervention consisting of filling holes with copper mesh, vacuuming and cleaning, and using low-toxicity pesticides and traps. Median levels in intervention homes fell to 2.8 μ g/g in kitchens, 2.2 μ g/g in bedrooms, and 0.9 μ g/g in living rooms at month 5.

4.4 Mold and Moisture

Various guidance documents for remediation of mold contamination have been developed.

- The New York City Department of Health has a set of guidelines, "Assessment and Remediation of Fungi in Indoor Environments," that are widely recognized. The document, originally developed for *Stachybotrys* but expanded to be inclusive of all molds, addresses health effects, environmental assessment, remediation techniques, and hazard communication (available at <u>http://www.nyc.gov/html/doh/html/epi/moldrpt1.html</u>).
- The Institute of Inspection Cleaning and Restoration Certification produced guideline S500: Standard and Reference Guide for Professional Water Damage Restoration (available by contacting the IICRC headquarters at (360) 693-5675 or through e-mail at <u>supplies@iicrc.org</u>).

- The American Conference of Governmental Industrial Hygienists (ACGIH) bioaerosols committee published in 1999, "Biosaerosols: Assessment and Control," a compilation of information on investigation strategies, sampling and analysis, and control of indoor bioaerosols, including molds (can be ordered through ACGIH at <u>http://www.acgih.org/home.htm</u>).
- The American Industrial Hygiene Association (AIHA) is in the process of developing a document with explicit guidelines for mitigation of mold hazards and some general guidelines for "clearance."
- U.S. Environmental Protection Agency published guidance for "Mold Remediation in Schools and Commercial Buildings," which includes many general principles also applicable to residential mold mitigation efforts (available through EPA at <u>http://www.epa.gov/iaq/molds/mold_remediation.html</u>).
- U.S. Environmental Protection Agency published guidance, "A Brief Guide to Mold, Moisture, and Your Home," for homeowners and renters on how to clean up residential mold problems and how to prevent mold growth (available from EPA online at <u>http://www.epa.gov/iaq/molds/images/moldguide.pdf</u>).
- The Canada Mortgage and Housing Corporation published, "Clean-up Procedures for Mold in Houses," which provides qualitative guidance for mold mitigation. (can be ordered from CMHC at <u>https://www.cmhc-</u> <u>schl.gc.ca:50104/b2c/b2c/init.do?language=en</u>)
- Health Canada published its "Fungal Contamination in Public Buildings" guide to assist investigators in recognizing and managing fungal contamination (available through Health Canada at <u>http://www.hc-sc.gc.ca/hecs-</u> <u>sesc/air_quality/pdf/fungal.pdf</u>).
- The Institute of Medicine of the National Academies report, *Damp Indoor Spaces and Health*, provides a summary of mitigation methods for mold (IOM, 2004).
- The Centers for Disease Control and Prevention recently published a report entitled "Mold: Prevention Strategies and Possible Health Effects in the Aftermath of Hurricanes Katrina and Rita," which provides advice on responses to flooded homes with an emphasis on worker protection (CDC, 2005).

Common intervention methods reported in the literature for residential mitigation of mold hazards include:

- Location and removal of sources of moisture (control of dampness and humidity and repair of water leakage problems).
- Increasing ventilation.

- Cleaning of mold contaminated materials that can be salvaged.
- Physical removal of materials with severe mold growth.
- Use of high-efficiency particulate air (HEPA) filters.
- Maintenance of heating, ventilation, and air conditioning systems.
- Prevention of spore infiltration from outdoors by closing doors and windows and by using air conditioning.

Because one of the most important factors affecting mold growth in homes (as well as other asthma related triggers such as dust mites) is moisture level, controlling this factor is crucial in abatement strategies. It is critical to find the source of moisture and remove it. Many simple measures can significantly control moisture, for example: maintaining indoor relative humidity at less than 50% through the use of dehumidifiers, fixing water leakage problems, increasing ventilation in kitchens and bathrooms by using exhaust fans, venting clothes dryers to the outside, reducing the number of indoor plants, using air conditioning at times of high outdoor humidity, heating all rooms in the winter and adding heating to outside wall closets, and using a sump pump in basements prone to flooding (Bush and Portnoy, 2001; ACGIH, 1999).

Preliminary research indicates that construction remediation of the causes of moisture sources in homes may be effective in reducing indoor mold and symptomatic days of asthmatic children living in the homes, but results have been modest and the studies have been hampered by small samples sizes and/or methodological issues (Kercsmar et al., 2005).

When mold contamination does occur, non-porous (e.g., metals, glass, and hard plastics) and semi-porous (e.g., wood and concrete) materials contaminated with mold and that are still structurally sound can often be cleaned with detergent or bleach solutions or by using quaternary amine preparations; however, in some cases, the material may not be easily cleaned or may be so severely contaminated that it may have to be removed. (Do not mix detergents and bleach. Some detergents have ammonia, which produces phosgene gas, a poisonous, suffocating gas, when mixed with bleach.) It is recommended that porous materials (e.g., ceiling tiles, wallboards, and fabrics) that cannot be cleaned be removed and discarded (NYC, 2000; USEPA, 2001). Physical removal interventions have proven effective, although additional research is needed regarding the containment of mold spores during the renovation process (NAS, 2000). It is recommended that rooms being remediated be isolated, using plastic sheeting, from the remainder of the home.

The use of biocides is discouraged by many experts because little research has been conducted on their effectiveness for this use and because of the potential human health hazards associated with this use (USEPA, 1997b; Foarde, 1998; Cole and Foarde, 1999). In addition, research indicates that dead mold material often retains the allergenic or toxic properties of the mold (Foarde, 1998; NAS, 2000), and thus removal is often cited as the best mitigation option.

When conducting cleaning or removal of mold contaminated materials in homes, worker protection is required. Activities such as cleaning or removal of mold-contaminated materials in homes, as well as investigations of mold contamination extent, have the potential to disturb areas of mold growth and release fungal spores and fragments into the air. This suggests that residents should not attempt repairs without the proper protection, or preferably should employ a contractor

trained in environmental remediation (Vesper et al., 2000). Recommended measures to protect workers during mold remediation efforts depend on the severity and nature of the mold contamination being addressed, but include the use of well fitted particulate masks or respirators that retain particles as small as 1µm or less, disposable gloves and coveralls, and protective eyewear (ACGIH, 1999).

For further information on mold remediation, see the HUD background paper, "Healthy Homes Issues: Mold."

4.5 Indoor Chemical Air Pollutants

Occupant choice plays the primary role in determining indoor exposure to environmental tobacco smoke (ETS). Caregivers and other household members can be urged to quit smoking or to smoke outside, and those with contact with the patient can be urged to wear a smoking jacket if they continue to smoke and/or to wash smoke-contaminated clothing that may come in contact with the patient. But engendering such behavioral change is difficult. Room air cleaners have been shown to be effective in reducing tobacco-smoke particles in the air (American Lung Association, 1997).

Reduction of pesticide exposure in the home can be achieved through alteration of consumer behavior and implementation of practices such as integrated pest management. Other indoor pollutants, such as emissions from products (e.g., phthalates) or appliances, may be minimized with changes in product use (e.g., using paints formulated to have low VOC emissions and pressed woods with reduced formaldehyde content) and increased ventilation (e.g., increasing the overall home air exchange rate and installing ventilation fans in areas containing sources) (NAS, 2000). Regular inspection of gas and wood burning appliances, correction of improper appliance ventilation systems, and installation of ventilation systems where unvented sources are present (e.g., unvented stoves in the kitchen), can reduce the potential hazard associated with emissions (including nitrogen and sulfur oxides, VOCs, CO, and particulates) from these sources. For example, in the National Cooperative Inner-City Asthma Study (NCICAS), air-monitoring measurements indicated that levels of nitrogen dioxide in inner-city homes investigated were often in excess of EPA environmental standards. These high levels, which could be expected to contribute to asthma aggravation, were thought to be related to gas use for 89% of the families and to the fact that 24% of the kitchens did not have functioning windows (Eggleston, 2000, citing Kattan et al., 1997).

5.0 CURRENT RESEARCH AND INFORMATION GAPS

Possible areas of consideration for future research include:

Methodological Issues Related to Assessment

- Determination of performance criteria for analytic methods (e.g., detection limits, etc.).
- Relation of environmental samples (vacuum dust, etc.) to actual exposure.
- Research on accuracy of home allergen tests and development of better sampling and quantitation techniques.

- Standardized methods for assessment and measurement of fungal allergens.
- Standardization of assays for measuring allergen levels to allow for comparison.
- Characterization of sources of variability in analytical results and development of quality control samples.
- Assessment of correlation between visual inspection methods and environmental sampling.

Methodological Issues Related to Mitigation

- Research on the relative cost-effectiveness of different intervention strategies and prioritization of mitigation alternatives.
- Research on the effect of insecticides on allergen levels (for dust mites and cockroaches) and effective methods of clean up after use of insecticides.
- Establishment of standards of quality for indoor allergen control products.
- Effectiveness of integrated pest management methods for controlling cockroach levels.
- Feasibility of effectively reducing cockroach allergen levels below thresholds.

Health and Exposure Issues

- Identification of threshold levels for sensitization to major residential allergens and for asthma exacerbation.
- Additional data on the role of rodent allergen exposure, particularly in socially disadvantaged populations.
- Information on additional allergens and irritants of importance in the home.
- Information on the relationship between indoor exposure to pesticides and exacerbation of asthma.
- Feasibility of preventing childhood sensitization to allergens through intervention.
- Policy and cost implications of preventing asthma by intervening in the home environment at birth.
- Information on factors that affect exposure, including research on how risk factors vary by location, or by housing or population characteristics.
- Research on the "hygiene hypothesis" and potential effects on intervention methods.
- Intervention studies in which pets are removed from the home to determine the effect of removal on asthma development.
- Additional data on the health effectiveness of moisture and mold reduction.
- Impact of the infiltration of outdoor air pollutants to indoors.

Issues Related to Housing Structure

- Data to quantify which aspects of household water damage are related to respiratory illness.
- Health impacts of building design and management.
- Areas of potential impact in building code and design to improve the indoor environment for asthmatics.
- Improved labeling of health building materials and home furnishings.

References

ACGIH. 1999. Bioaerosols: Assessment and Control. (J. Macher, ed.). American Conference of Governmental and Industrial Hygienists, Cincinnati, Ohio.

Aligne, C.A., Auinger, P., Byrd, R.S., Weitzman, M. 2000. Risk factors for pediatric asthma: Contribution of poverty, race, and urban residence. American Journal of Respiratory and Critical Care Medicine. 162: 873-877.

American Academy of Pediatrics Committee on Environmental Health. 1998. Toxic effects of indoor molds. Pediatrics. 101: 712-714.

American Lung Association. 1997. Residential Air Cleaning Devices. Available at http://www.lungusa.org.

Apter, A.J. 2003. Early exposure to allergen: Is this the cat's meow, or are we barking up the wrong tree? Journal of Allergy and Clinical Immunology. 111(5):938-46.

Arlian, L.G., Neal, J.S., Morgan, M.S., Vyszenski-Moher, D., Rapp, C.M., and Alexander, A.K. 2001. Reducing relative humidity is a practical way to control dust mites and their allergens in homes in temperate climates. Journal of Allergy and Clinical Immunology. 107(1):99-104.

Alm, J.S., Swartz, J., Lilja, G., Scheynius, A., and Pershagen, G. 1999. Atopy in children of families with an anthroposophic lifestyle. Lancet. 353:1485-88.

Arbes, S.J., Cohn, R.D., Yin, M., Muilenberg, M.L., Burge, H.A., Friedman, W., and Zeldin, D.C. 2003a. House dust mite allergen in U.S. beds: Results from the first National Survey of Lead and Allergens in Housing. Journal of Allergy and Clinical Immunology. 111(2):408-14.

Arbes, S.J., Sever, M., Archer, J., Long, E.H., Gore, J.C., Schal, C., Walter, M., Neubler, B., Vaughn, B., Mitchell, H., Liu, E., Collette, N., Adler, P., Sandel, M., and Zeldin, D.C. 2003b. Abatement of cockroach allergen (Bla g 1) in low-income, urban housing: A randomized controlled trial. Journal of Allergy and Clinical Immunology. 112(2):339-45.

Arbes, S.J., Sever, M., Mehta, J., Gore, J.C., Schal, C., Vaughn, B., Mitchell, H., and Zeldin, D.C. 2004. Abatement of cockroach allergens (Bla g 1 and Bla g 2) in low-income, urban housing: Month 12 continuation results. Journal of Allergy and Clinical Immunology. 113(1):109-14.

Arruda, K.L., Vailes, L.D., Ferriani, V.P., Santos, A.B., Pomes, A., and Chapman, M.D. 2001. Cockroach allergens and asthma. Journal of Allergy and Clinical Immunology. 107(3): 419-427.

ASTM E 1728-95. 1995. Standard practice for the field collection of settled dust samples using wipe sampling methods for lead determination by atomic spectrometry techniques. American Society of Testing and Materials, Philadelphia, PA.

Ball, T.M., Castro-Rodriguez, J.A., Griffith, K.A., Holberg, C.J., Martinez, F.D., and Wright, A.L. 2000. Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. New England Journal of Medicine. 343:538-543.

Becher, R., Hongslo, J.K., Jantunen, M.J., and Dybing, E. 1996. Environmental chemicals relevant for respiratory hypersensitivity: the indoor environment. Toxicology Letters. 86:155-162.

Belanger, K., Beckett, W., Triche, E., Bracken, M.B., Holford, T., Ren, P., McSharry, J., Gold, D.R., Platts-Mills, T.A.E., and Leaderer, B.P. 2003. Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma. American Journal of Epidemiology. 158:195-202.

Bergmann, R.L., Niggemann, B., and Wahn, U. 1998. Allergen avoidance should be first line treatment for asthma. Eur Resp Rev. 8(53):161-163.

Braun-Fahrlander, C., Riedler, J., Herz, U., Eder, W., Waser, M., Grize, L., Maisch, S., Carr, D., Gerlach, F., Bufe, A., Lauener, R.P., Schierl, R., Renz, H., Nowak, D., and von Mutius, E. 2002. Environmental exposure to endotoxin and its relation to asthma in school-age children. New England Journal of Medicine. 347(12):869-877.

Brenner, B.L., Markowitz, S., Rivera, M., Romero, H., Weeks, M., Sanchez, E., Deych, E., Garg, A., Godbold, J., Wolff, M.S., Landrigan, P.J., and Berkowitz, G. 2003. Integrated pest management in an urban community: A successful partnership for prevention. Environmental Health Perspectives. 111(13):1649-1653.

Bornehag, C.G., Sundell, J., Weschler, C.J., Sigsgaard, T., Lundgren, B., Hasselgren, M., and Hagerhed-Engman, L. 2004. The association between asthma and allergic symptoms in children and phthalates in house dust: A nested case-control study. Environmental Health Perspectives. 112:1393-1397.

Bornehag, C.G., Lundgren, B., Weschler, C. J., Sigsgaard, T., Hagerhed-Engman, L., and Sundell, J. 2005. Phthalates in indoor dust and their association with building characteristics. Environmental Health Perspectives. 113(10):1399-1404.

Burge, H.A. and Ammann, H.A. 1999. Fungal toxins and β (1 \rightarrow 3)-D-glucans. In: Bioaerosols: Assessment and Control. (J. Macher, ed.). American Conference of Governmental and Industrial Hygienists, Cincinnati, Ohio.

Burge, H.A. and Otten, J.A. 1999. Fungi. In: Bioaerosols: Assessment and Control. (J. Macher, ed.). American Conference of Governmental and Industrial Hygienists, Cincinnati, Ohio.

Bush, R.K. and Portnoy, J.M. 2001. The role and abatement of fungal allergens in allergic diseases. Journal of Allergy and Clinical Immunology (Supplement). 107(3, part 2): 430.

Campbell, M.E., Dwyer, J.J., Goettler, F., Ruf, F., and Bittiglio, M. 1999. A program to reduce pesticide spraying in the indoor environment: Evaluation of the 'Roach Coach' project. Canadian Journal of Public Health. 90(4):277-281.

Carter, S.E. and Platts-Mills, T.A. 1998. Searching for the cause of the increase in asthma. Current Opinion in Pediatrics. 10:594-9.

CDC. 1998a. Forecasted state-specific estimates of self-reported asthma prevalence -- United States, 1998. MMWR. December 04, 1998: 47(47):1022-1025.

CDC. 1998b. Surveillance for asthma -- United States, 1960-1995. In: CDC Surveillance Summaries, MMWR. April, 1998: 47(no. SS-1).

CDC. 2003. Asthma FAQ: Basic Facts about Asthma. Available online at: <u>http://www.cdc.gov/nceh/airpollution/asthma/faqs.pdf</u>

CDC, 2005. Centers for Disease Control and Prevention, National Center for Environmental Health, National Center for Infectious Diseases, National Institute for Occupational Safety and Health, "Mold: Prevention Strategies and Possible Health Effects in the Aftermath of Hurricanes Katrina and Rita," Department of Health and Human Services, October 2005.

Celedon, J.C., Litonjua, A.A., Ryan, L., Platts-Mills, T., Weiss, S.T., and Gold, D.R. 2002. Exposure to cat allergen, maternal history of asthma, and wheezing in first 5 years of life. Lancet. 360: 781-82.

Celedon, J.C., Wright, R.J., Litonjua, A.A., Sredl, D., Ryan, L., Weiss, S.T., and Gold, D.R. 2003. Day care attendance in early life, maternal history of asthma, and asthma at the age of 6 years. American Journal of Respiratory and Critical Care Medicine. 167(9):1239-43.

Chan-Yeung, M., Ferguson, A., Watson, W., Dimich-Ward, H., Rousseau, R., Lilley, M., DyBuncio, A., and Becker, A. 2005. The Canadian Childhood Asthma Primary Prevention Study: Outcomes at 7 years of age. Journal of Allergy Clinical Immunology. 116:49-55.

Chapman, M. D. 1998. Environmental allergen monitoring and control. Allergy 53:48-53.

Chapman, M.D. and Wood, R.A. 2001. The role and remediation of animal allergens in allergic diseases. Journal of Allergy and Clinical Immunology. 107:S414-421.

Chapman, M.D., Vailes, L.D., and Ichikawa, K. 2000. Immunoassays for Indoor Allergens. Clinical Reviews in Allergy & Immunology 18(3):285-300.

Chapman, M.D., Vailes, L.D., Hayden, M.L., Platts-Mills, T.A.E., and Arruda, L.K. 1997. Cockroach allergens and their role in asthma. In: Allergy and Allergic Diseases. pp. 942-953 A.B. Kay, Blackwell Science, Oxford.

Chew, G. L., Higgins, K.M., Gold, D.R., Muilenberg, M.L., and Burge, H.A. 1999. Monthly measurements of indoor allergens and the influence of housing type in a northeastern US city. Allergy 54:1058-1066.

Chew, G.L., Burge, H.A., Dockery, D.W., Muilenberg, M.L., Weiss, S.T. and Gold, D.R. 1998. Limitations of a home characteristics questionnaire as a predictor of indoor allergen levels. American Journal of Respiratory and Critical Care Medicine. 157:1536-1541.

Chew, G.L., Perzanowski, M.S., Miller, R.L., Correa, J.C., Hoepner, L.A., Jusino, C.M., Becker, M.G., and Kinney, P.L. 2003. Distribution and determinants of mouse allergen exposure in low-income New York City apartments. Environmental Health Perspectives. 110(10):1348-1351.

Clickner, R.P., Marker, D., Viet, S.M., Rogers, J., Broene, P. 2001. National Survey of Lead and Allergens in Housing. Volume I: Analysis of Lead Hazards, Final Draft. Prepared for: U.S. Department of Housing and Urban Development (HUD).

CMHC. 1998. Farewell To Cockroaches: Getting Rid of Cockroaches the Least-Toxic Way. Canada Mortgage and Housing Corporation. Canada. Available online at: <u>http://www.cmhc-schl.gc.ca/en/burema/gesein/faroach/faroach_011.cfm</u>

Cole, E.C. and Foarde, K.K. 1999. Biocides and Antimicrobial Agents. In: Bioaerosols: Assessment and Control. (J. Macher, ed.). American Conference of Governmental and Industrial Hygienists, Cincinnati, Ohio.

Cohn, R.D., Arbes, S.J.Jr., Jaramillo, R., Reid, L.H., and Zeldin, D.C. National prevalence and exposure risk for cockroach allergen in US households. Environmental Health Perspectives. Online 15 November 2005.

Curtis, L., Ross, M., Scheff, P., Persky, V., Wadden, R., Ramakrishnan, V., and Hryhorczuk, D. 1997. Dust-mite-allergen concentrations in asthmatics' bedrooms in the Quad Cities (Illinois, USA) after the Mississippi River floods of 1993. Allergy. 52:642-649.

Custovic, A., Smith, A. and Woodcock, A. 1998a. Indoor allergens are a primary cause of asthma. European Respiratory Review. 8(53):155-158.

Custovic, A., Fletcher, A., Pickering, C.A., Francis, H.C., Green, R., Smith, A., et al. 1998b. Domestic allergens in public places III: house dust mite, cat, dog and cockroach allergens in British hospitals. Clinical and Experimental Allergy. 28:53-9.

De Lucca, S. et al. 1998. Mite allergen (Der p 1) is not only carried on feces. J. Allergy Clinical Immunology. 101: S168.

DeWeck, A.L., Derer, M., Morrison-Smith, G., Stadler, B.M., and Walliser, M. 1998. Dustscreen, a new assay for simultaneous determination of multiple allergens in house dust. ACI International. 10:133-140.

Dillon, H.K., Miller, J.D., Sorenson, W.G., Douwes, J., and Jacobs, R.R. 1999. Review of methods applicable to the assessment of mold exposure to children. Environmental Health Perspectives. 107(Suppl. 3): 473-480.

Eggleston, P.A. 2000. Environmental causes of asthma in inner city children. Clinical Reviews of Allergy & Immunology. 18(3):311-324.

Eggleston, P.A. 2003. Control of environmental allergens as a therapeutic approach. Immunology and Allergy Clinics of North America. 23:533-547.

Eggleston, P.A. and Arruda, L.K. 2001. Ecology and elimination of cockroaches and allergens in the home. Journal of Allergy and Clinical Immunology (Supplement). 107(3, part 2):422.

Eggleston, P.A., Buckley, T.J., Breysse, P.N., Wills-Karp, M., Kleeberger, S.R., and Jaakkola, J.J.K. 1999a. The environment and asthma in U.S. inner cities. Environmental Health Perspectives. 107(S3): 439-450.

Eggleston, P.A., Wood, R.A., Rand, C., Nixon, W.J., Chen, P.H., Lukk, P. 1999b. Removal of cockroach allergen from inner city homes. Journal of Allergy and Clinical Immunology. 104:842-846.

Erwin, E.A., Woodfolk, J.A., Custis, N., and Platts-Mills, T.A.E. 2003. Animal danders. Immunology and Allergy Clinics of North America. 23:469-481.

Etzel, R.A. 2000. The "fatal four" indoor air pollutants. Pediatric Annals. 29(6):344-50.

Etzel, R. A. 1995. Indoor air pollution and childhood asthma: Effective environmental interventions. Environmental Health Perspectives. 103(6), 7pp.

Farfel, M., Chisolm, J. Jr., Orlova, A., Brophy, M., and Litt, J. 2000. An Extended Study of Interim Lead Hazard Reduction Measures Employed In The Baltimore Clinical Center of The Treatment Of Lead-Exposed Children (TLC)-Clinical Trial April 2000. Prepared for: U.S. Dept. of Housing and Urban Development, Office of Healthy Homes and Lead Hazard Control.

Findley, S., Lawler, K., Bindra, M., Maggio, L., Penachio, M.M., and Maylahn, C. 2003. Elevated asthma and indoor environmental exposures among Puerto Rican children of East Harlem. Journal of Asthma. 40(5):557-69.

Flannigan, B. 1997. Air sampling for fungi in indoor environments. Journal of Aerosol Science. 28(3):381-392.

Foarde, K.K. 1998. Proper use of biocides in HVAC systems. National Air Duct Cleaners (NADCA) 9th Annual Meeting & Exposition, 1998. Research Triangle Institute.

Frantz, S.C., Gronning, E.K., and Chaput, R.L. 1999. Designing integrated pest management for the sustained reduction of cockroach and rodent populations for asthma prevention in low-income urban residences. National Environmental Health Association's 63rd Annual Educational Conference & Exhibition, Nashville, TN, July 6-9, 1999.

Garrett, M.H., Hooper, M.A., Hooper, B.M., Rayment, P.R., and Abramson, M.J. 1999. Increased risk of allergy in children due to formaldehyde exposure in homes. Allergy. 54:330-337.

Gent, J.F., Ren, P., Belanger, K., Triche, E., Bracker, M.B., Holford, T.R., and B.P. Leaderer. 2002. Levels of household mold associated with respiratory symptoms in the first year of life in a cohort at risk for asthma. Environmental Health Perspectives. 110(12): A781-786.

Gergen, P.J., Mortimer, K.M., Eggleston, P.A., Rosenstreich, D., Mitchell, H., Ownby, D., Kattan, M., Baker, D., Wright, E.C., Slavin, R. and Malveaux, F. 1999. Results of the National Cooperative Inner-City Asthma Study (NCICAS) environmental intervention to reduce cockroach allergen exposure in inner-city homes. Journal of Allergy and Clinical Immunology. 103(3):501-506

Gergen, Peter J. Personal communication. 11/28/2000. U.S. Agency for Healthcare Research and Quality (AHRQ), Department of Health and Human Services.

Gravesen, S. 1999. Microfungal contamination of damp buildings: Examples of risk construction and risk materials. Environmental Health Perspectives. 107(3): 505-508.

Gruchalla, R.S., Pongracic, J., Plaut, M., Evans, R.III, Visness, C. M., Walter, M., Crain, E.F., Kattan, M., Morgan, W.J., Steinbach, S., Stout, J., Malindzak, G., Smartt, E., and Mitchell, H. 2005. Inner City Asthma Study: Relationships among sensitivity, allergen exposure, and asthma morbidity. Journal of Allergy and Clinical Immunology. 115(3):478-85.

Hartert, T.V. and Peebles, R.S. Jr. 2000. Epidemiology of asthma: the year in review. Current Opinion in Pulmonary Medicine. 6:4-9.

Hesselmar, B., Aberg, N., Aberg, B., Eriksson, B., and Bjorksten, B. 1999. Does early exposure to cat or dog protect against later allergy development? Clinical and Experimental Allergy. 29:611-617.

Hirsch, T., Kuhlisch, E., Soldan, W., and Leupold, W. 1998. Variability of house dust mite allergen exposure in dwellings. Environmental Health Perspectives. 106(10):659.

HUD. 2004a. HUD Office of Healthy Homes and Lead Hazard Control, "Vacuum Dust Sample Collection Protocol for Allergens," April 30, 2004.

HUD. 2004b. HUD Office of Healthy Homes and Lead Hazard Control, "Background and Justification for a Vacuum Sampling Protocol for Allergens in Household Dust," April 30, 2004.

Huss, K., Naumann, P.L., Mason, P.J., Nanda, J.P., Huss, R.W., Smith, C.M., and Hamilton, R.G. 2001a. Asthma severity, atopic status, allergen exposure and quality of life in elderly persons. Annals of Allergy, Asthma and Immunology. 86(5):524-30.

Huss, K., Adkinson, N.F. Jr., Eggleston, P.A., Dawson, E., Van Natta, M.L., and Hamilton, R.G. 2001b. House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program. Journal of Allergy and Clinical Immunology. 107(1):48-54.

IOM. 2004. Damp Indoor Spaces and Health. Institute of Medicine of the National Academies, Board on Health Promotion and Disease, Committee on Damp Indoor Spaces and Health. The National Academies Press, Washington, DC.

Ingram, J.M., Sporik, R., Rose, G., Honsinger, R., Chapman, M.D., and Platts-Mills T.A.E. 1995. Quantitative assessment of exposure to dog (Can f 1) and cat (Fel d 1) allergens: relationship to sensitization and asthma among children living in Los Alamos, New Mexico. Journal of Allergy and Clinical Immunology. 96:449-456.

ISAAC Steering Committee (The International Study of Asthma and Allergies in Childhood). 1998. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. Lancet. 351:1225-1232.

Jacob, B., Ritz, B., Gehring, U., Koch, A., Bischof, W., Wichmann, H.E., and Heinrich, J. for the INGA-Study Group. 2002. Indoor exposure to molds and allergic sensitization. Environmental Health Perspectives. 110:647-653.

Karmaus, W. and Botezan, C. 2002. Does a higher number of siblings protect against the development of allergy and asthma? A review. Journal of Epidemiology and Community Health. 56(3):209-17.

Katial, R.K. 2003. Cockroach allergy. Immunology and Allergy Clinics of North America. 23: 483-499.

Kattan, M., Stearns, S.C., Crain, E.F., Stout, J.W., Gergen, P.J., Evans, R., Visness, C.M., Gruchalla, R.S., Morgan, W.J., O'Connor, G.T., Mastin, J.P., and Mitchell, H.E. 2005. Cost-effectiveness of a home-based environmental intervention for inner-city children with asthma. Journal of Allergy and Clinical Immunology. 116(5):1058-63.

Kattan, M., Mitchell, P. Eggleston, P.A. et al. 1997. Characteristics of inner-city children with asthma: the National Cooperative Inner-City Asthma Study. Pediatric Pulmonology. 24:253-262.

Kercsmar, C.M., Dearborn, D.G., Schluchter, M., Xue, L., Kirchner, H.L., Sobelewski, J., Greenberg, S.J., Vesper, S.J., and Allan, T. 2005. Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. Submitted for publication.

Kitch, B.T., Chew, G., Burge, H.A., Muilenberg, M.L., Weiss, S.T., Platts-Mills, T.A.E., O'Connor, G., and Gold, D.R.. 2000. Socioeconomic predictors of high allergen levels in homes in the greater Boston area. Environmental Health Perspectives. 108(4):12pp.

Klinnert, M.D., Liu, A.H., Pearson, M.R., Ellison, M.C., Budhiraja, N., and Robinson, J.L. 2005. Short-term impact of a randomized multifaceted intervention for wheezing infants in low-income families. Archives of Pediatrics & Adolescent Medicine. 159:75-82.

Krieger, J.W., Takaro, T.K., Song, L., and Weaver, M. 2005. The Seattle-King County Healthy Homes Project: A randomized, controlled trial of a community health worker intervention to decrease exposure to indoor asthma triggers. American Journal of Public Health. 95(4):652-9.

Lanphear, B.P., Aligne, C.A., Auinger, P., Weitzman, M., and R.S. Boyd. 2001. Residential exposures associated with asthma in US children. Pediatrics. 107(3):505-511.

Leaderer, B.P., Belanger, K., Triche, E., Holford, T., Gold, D.R., Kim, Y., Jankun, T., Ren, P., McSharry, J., Platts-Mills, T.A.E., Chapman, M.D., and Bracken, M.B. 2002. Dust mite, cockroach, cat, and dog allergen concentrations in homes of asthmatic children in the northeastern United States: impact of socioeconomic factors and population density. Environmental Health Perspectives. 110(4):419-425.

Levy, J.I., Brugge, D., Peters, J.L., Clougherty, J.E., Saddler, S.S. 2005. A community-based participatory research study of the efficacy of multifaceted in-home environmental interventions for pediatric asthmatics in public housing. Submitted for publication.

Li, J.T. 2002. Allergy testing. American Family Physician. 66(4):621-624.

Litonjua, A.A., Carey, V.J., Burge, H.A. Weiss, S.T., and Gold, D.R. 2001. Exposure to cockroach allergen in the home is associated with incident doctor-diagnosed asthma and recurrent wheezing. Journal of Allergy and Clinical Immunology. 107:41-47.

Litonjua, A.A., Carey, V.J., Weiss, S.T., and Gold, D.R. 1999. Race, socioeconomic factors, and area of residence are associated with asthma prevalence. Pediatric Pulmonology. 28:394-401.

Liu, A.H. and Szefler, S.J. 2003. Advances in childhood asthma: hygiene hypothesis, natural history, and management. Journal of Allergy and Clinical Immunology. 111(3 Suppl): S785-92.

Mahooti-Brooks, N., Storey, E., Yang, C., Simcox, N.J., Turner, W., and Hodgson, M. 2004. Characterization of mold and moisture indicators in the home. Journal of Occupational and Environmental Hygiene. 1(12):826-39.

Martyny, J., Martinez, K.F. and Morey, P.R. 1999. Source sampling. In: Bioaerosols: Assessment and Control. (J. Macher, ed.). American Conference of Governmental and Industrial Hygienists, Cincinnati, Ohio.

Matsui, E.C., Wood, R.A., Rand, C., Kanchanaraksa, S., Swartz, L., Curtin-Brosnan, J., and Eggleston, P.A. 2003. Cockroach allergen exposure and sensitization in suburban middle-class children with asthma. Journal of Allergy and Clinical Immunology. 112(1):87-92.

Meklin, T., Haugland, R.A., Reponen, T., Varma, M., Lummus, Z., Bernstein, D., Wymer, L.J., and Vesper, S.J. 2004. Quantitative PCR analysis of house dust can reveal abnormal mold conditions. Journal of Environmental Monitoring. 6(7):615-20.

Michel, O., Kips, J., Duchateau, J., Vertongen, F., Robert, L., Collet, H., Pauwels, R., and Sergysels, R. 1996. Severity of asthma is related to endotoxin in house dust. American Journal of Respiratory and Critical Care Medicine. 154(6 Pt 1):1641-1646.

Mihrshahi, S., Marks, G.B., Criss, S., Tovey, E.R., Vanlaar, C.H., and Peat, J.K. for the CAPS Team. 2003. Effectiveness of an intervention to reduce house dust mite allergen levels in children's beds. Allergy. 58:784-789.

Miller, D.M., Meek, F. 2004. Cost and efficacy comparison of integrated pest management strategies with monthly spray insecticide applications for German cockroach (Dictyoptera: Blattellidae) control in public housing. Journal of Economic Entomology. 97(2):559-69.

Miller, R.L., Garfinkel, R., Horton, M., Camann, D., Perera, F.P., Whyatt, R.M., and Kinney, P.L. 2004. Polycyclic aromatic hydocarbons, environmental tobacco smoke, and respiratory symptoms in an inner-city birth cohort. Chest. 126:1071-1078.

Mistrello, G. et al. 1998. Dot immunobinding assay for the detection of mite allergens in house dust samples. Journal of Medical Entomology. 35:143-147.

Morgan, W.J., Crain, E.F., Gruchalla, R.S., O'Connor, G.T., Kattan, M., Evans, R. III, Stout, J., Malindzak, G., Smartt, E., Plaut, M., Walter, M., Vaughn, B., and Mitchell, H. 2004. Results of a home-based environmental intervention among urban children with asthma. The New England Journal of Medicine. 351:1068-1080.

NAS. 2000. Clearing the Air: Asthma and Indoor Air Exposures. National Academy of Sciences' Institute of Medicine, Division of Health Promotion and Disease Prevention. National Academy Press, Washington, D.C. 438 pp.

NYC. 2000. Guidelines on Assessment and Remediation of Fungi in Indoor Environments. New York City Department of Health, Bureau of Environmental & Occupational Disease Epidemiology. Available online: <u>http://www.ci.nyc.ny.us/html/doh/html/epi/moldrpt1.html</u>

Ogg, B., Ferraro, D., and Ogg, C. 1994. Cockroach Control Manual. University of Nebraska-Lincoln, Institute of Agriculture and Natural Resources, Lancaster County Cooperative Extension Office. Lincoln, NE. Available online at <u>http://pested.unl.edu/cockcom.htm</u>

O'Meara, T. and Tovey, E. 2000. Monitoring personal allergen exposure. Clinical Reviews in Allergy & Immunology. 18(3):341-395.

O'Meara, T.J., DeLucca, S., Sporik, R., Graham, A., and Tovey, E. 1998. Detection of inhaled cat allergen. Lancet. 351:1488-1489.

Pandya, R.J., Solomon, G., Kinner, A., and Balmes, J.R. 2002. Diesel exhaust and asthma: hypotheses and molecular mechanisms of action. Environmental Health Perspectives. 110 Suppl 1:103-12.

Park, J.-H., Schleiff, P.L., Attfield, M.D., Cox-Ganser, J.M., and Kreiss, K. 2004. Buildingrelated respiratory symptoms can be predicted with semi-quantitative indices of exposure to dampness and mold. Indoor Air. 14(6):425-33.

Pate, A.D., Hamilton, R.G., Ashley, P.J., Zeldin, D.C., and Halsey, J.F. 2005. Proficiency testing of allergen measurements in residential dust. Journal of Allergy and Clinical Immunology. 116:844-50.

Perera, F.P., Rauh, V., Tsai, W-Y., Kinney, P., Camann, D., Barr, D., Bernert, T., Garfinkel, R., Tu, Y-H., Diaz, D., Dietrich, J., and Whyatt, R.M. 2003. Effects of transplacental exposure to environmental pollutants on birth outcomes in a multiethnic population. Environmental Health Perspectives. 111(2):201-205.

Perry, T., Matsui, E., Merriman, B., Duong, T., and Eggleston, P. 2003. The prevalence of rat allergen in inner-city homes and its relationship to sensitization and asthma morbidity. Journal of Allergy and Clinical Immunology. 112(2):346-52.

Phipatanakul, W., Eggleston, P.A., Wright, E.C., Wood, R.A., and National Cooperative Inner-City Asthma Study. 2000a. Mouse allergen. I. The prevalence of mouse allergen in inner-city homes. Journal of Allergy and Clinical Immunology. 106(6):1070-1074.

Phipatanakul, W., Eggleston, P.A., Wright, E.C., Wood, R.A., and National Cooperative Inner-City Asthma Study. 2000b. Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. Journal of Allergy and Clinical Immunology. 106(6):1075-1080.

Phipatanakul, W., Cronin, B., Wood, R.A., Eggleston, P.A., Shih, M-C., Song, L., Tachdjian, R., Oettgen, H.C. 2004. Effect of environmental intervention on mouse allergen levels in homes of inner-city Boston children with asthma. Annals of Allergy, Asthma, & Immunology. 92:420-5.

Platts-Mills, T.A.E. 1998. Changes in the 20th century environment: Do they explain the increase in asthma? Presented at the NAIAD Symposium: Asthma and the Environment. National Institute of Allergy and Infectious Disease. March 14, 1998.

Platts-Mills, T.A., Vaughan, J., Squillace, S., Woodfolk, J., and Sporik, R. 2001. Sensitization, asthma, and a modified Th2 response in children exposed to cat allergen: A population-based cross-sectional study. The Lancet. 357: 752-756.

Platts-Mills, T. A., Rakes, G., and Heymann, P.W. 2000a. The relevance of allergen exposure to the development of asthma in childhood. Journal of Allergy and Clinical Immunology. 105(2 Pt 2):S503-8.

Platts-Mills, T.A., Vaughan, J.W., Carter, M.C. and Woodfolk, J.A. 2000b. The role of intervention in established allergy: Avoidance of indoor allergens in the treatment of chronic allergic disease. Journal of Allergy and Clinical Immunology. 106:787-804.

Platts-Mills, T.A. E., Vervloet, D., Thomas, W.R., Aalberse, R.C., and Chapman, M.D. 1997. Indoor Allergens and Asthma: Report of the Third International Workshop. Journal of Allergy and Clinical Immunology. 100(6, Part 1):S1-S23.

Platts-Mills, T.A., Sporik, R.B., Wheatley, L.M., and Haymann, P.W. 1995. Is there a dose-response relationship between exposure to indoor allergens and symptoms of asthma? Journal of Allergy and Clinical Immunology. 96(4): 435-440.

Poulos, L. et al. 1998. Detection of inhaled Der p 1 and Fel d 1. Journal of Allergy and Clinical Immunology. 101: S158.

Rao, C.Y., Burge, H.A., and Chang, J.C.S. 1996. Review of quantitative standards and guidelines for fungi in indoor air. J Air Waste Management Association. 46(9):899-908.

Ren, P., Jankun, T.M., Belanger, K., Bracken, M.B., and Leaderer, B.P. 2001. The relation between fungal propagules in indoor air and home characteristics. Allergy. 56:419-424.

Rogers, L., Cassino, C., Berger, K.I., Goldring, R.M., Norman, R. G., Klugh, T., and Reibman, J. 2002. Asthma in the elderly: cockroach sensitization and severity of airway obstruction in elderly nonsmokers. Chest. 122(5):1580-6.

Ronmark, E., Perzanowski, M., Platts-Mills, T., and Lundback, B. 2003. Four-year incidence of allergic sensitization among schoolchildren in a community where allergy to cat and dog dominates sensitization: report from the Obstructive Lung Disease in Northern Sweden Study Group. Journal of Allergy and Clinical Immunology. 112(4):747-54.

Smith, A.M. 1999. Molecular Structure, Function, and Immune System Response to Allergens. *In:* Indoor Allergens: From Theory to Practice. Charlottesville, VA.

Sporik, R., Squillace, S.P., Ingram, J.M., Rakes, G., Honsinger, R.W., and Platts-Mills, T.A. 1999. Mite, cat, and cockroach exposure, allergen sensitization, and asthma in children: A case-control study of three schools. Thorax. 54: 675-680.

Sporik, R., Ingram, J.M., Price, W., Sussman, J.H., Honsinger, R.W., and Platts-Mills, T.A.E. 1995. Association of asthma with serum IgE and skin-test reactivity to allergen among children living at high altitude: tickling the dragon's breath. American Journal of Respiratory and Critical Care Medicine. 151:1388-1392.

Takaro, T.K., Krieger, J.W., and Song, L. 2004. Effect of environmental interventions to reduce exposure to asthma triggers in homes of low-income children in Seattle. Journal of Exposure Analysis and Environmental Epidemiology. 14 Suppl 1:S133-43.

Thorne, P.S., Kulhankova, K, Yin, M, Cohn, R., Arbes, S.J. Jr., and Zeldin, D.C. 2005. Endotoxin exposure is a risk factor for asthma: the national survey of endotoxin in U.S. housing. American Journal of Respiratory and Critical Care Medicine. 172(11):1371-7.

Tovey, E. et al. 1998. A new in vitro diagnostic method. Journal of Allergy and Clinical Immunology. 101:S129.

Tsay, A., Williams, L., Chandler, J., and Chapman, M.D. 1999. Rapid test for mite allergen detection in the home. Journal of Allergy and Clinical Immunology. 103:S235.

USEPA. 1995. Sampling house dust for lead: basic concepts and literature review. U.S. Environmental Protection Agency. EPA 747-R-95-007.

USEPA. 1997a. Exposure factors handbook (Update). National Center for Environmental Assessment, Office of Research and Development. Washington, DC. EPA/600/P-95/002Fa.

USEPA. 1997b. Should You Have the Air Ducts in Your Home Cleaned? (EPA-402-K-97-002). Indoor Environments Division, Office of Air and Radiation (OAR), U.S. Environmental Protection Agency. October 1997.

USEPA Press Release. 2001. EPA Scientists Develop Technology For Detection Of Dangerous Molds. Released: 5/8/2001. Available through EPA website: <u>http://www.epa.gov/</u>

Vailes, L., Sridhara, S., Cromwell, O., Weber, B., Breitenbach, M., and Chapman, M. 2001. Quantitation of the major fungal allergens, Alt a 1 and Asp f 1, in commercial allergenic products. Journal of Allergy and Clinical Immunology . 104(4):641.

Van der Heide, S. van Aalderen, W.M., Kauffman, H.F., Dubois, A.E. and de Monchy, J.G. 1999. Clinical effects of air cleaners in homes of asthmatic children sensitized to pet allergens. Journal of Allergy and Clinical Immunology. 104(2 Pt 1):447-451.

Vaughan, J.W. and Platts-Mills, T.A. 2000. New Approaches to Environmental Control. Clinical Reviews in Allergy & Immunology. 18(3):325-339.

Vaughan, J.W., McLaughlin, T.E., Perzanowski, M.S., and Platts-Mills, T.A.E. 1999a. Evaluation of materials used for bedding encasement: Effect of pore size in blocking cat and dust mite allergen. Journal of Allergy and Clinical Immunology. 103(2):227-231.

Vaughan, J.W., Woodfolk, J.A. and Platts-Mills, T.A.E. 1999b. Assessment of vacuum cleaners and vacuum cleaner bags recommended for allergic subjects. Journal of Allergy and Clinical Immunology. 104(5):1079-1083.

Venn, A.J., Cooper, M., Antoniak, M., Laughlin, C., Britton, J., and Lewis, S.A. 2003. Effects of volatile organic compounds, damp, and other environmental exposures in the home on wheezing illness in children. Thorax. 58(11):955-60.

Vesper, S., Dearborn, D.G., Yike, I., Allan, T., Sobolewski, J., Hinkley, S.F., Jarvis, B.B., and Haugland, R.A. 2000. Evaluation of Stachybotrys chartarum in the house of an infant with pulmonary hemorrhage: quantitative assessment before, during, and after remediation. Journal of Urban Health: Bulletin of the New York Academy of Medicine. 77(1):68-85.

Vesper, S.J., Varma, M., Wymer, L.J., Dearborn, D.G., Sobolewski, J., and Haugland, R.A. 2004. Quantitative polymerase chain reaction analysis of fungi in dust from homes of infants who developed idiopathic pulmonary hemorrhaging. Journal of Occupational and Environmental Medicine. 46(6):596-601.

Vesper, S.J., McKinstry, C., Yang, C., Haugland, R., Kercsmar, C.M., Yike, I., Schluchter, M.D., Kirchner, H.L., Sobolewski, J., Allan, T.M., and Dearborn, D.G. 2005. Are specific molds associated with asthma in water-damaged homes? Submitted for publication.

Vojta, P.J., Randels, S.P., Stout, J., Muilenberg, M., Burge, H.A., Lynn, H., Mitchell, H., O'Connor, G.T., and Zeldin, D.C. 2001. Effects of physical interventions on house dust mite allergen levels in carpet, bed, and upholstery dust in low-income, urban homes. Environmental Health Perspectives. 109(8): 815-819.

Vojta, P.J., Friedman, W., Marker, D.A., Clickner, R., Rogers, J.W., Viet, S.M., Muilenberg, M.L., Thorne, P.S., Arbes, Jr., S.J., and Zeldin, D.C. 2002. First National Survey of Lead and Allergens in Housing: Survey design and methods for the allergen and endotoxin components. Environmental Health Perspectives. 110(5):527-532.

von Mutius, E. 2002. Environmental factors influencing the development and progression of pediatric asthma. Journal of Allergy and Clinical Immunology. 109(6 Suppl):S525-32.

Wang, E., Rhoads, G., Wainman, T., and Lioy, P.J. 1995. Effects of environmental and carpet variables on vacuum sampler collection efficiency. Applied Occupational and Environmental Hygiene. 10(2):111-119.

Wang, C., and Bennett, G.W. 2006. A comparative study of integrated pest management and baiting for German cockroach management in public housing. Journal of Economic Entomology. Vol. 99 (in print).

WHO/IUIS Allergen Nomenclature Subcommittee. 1994. Allergen Nomenclature. (Hoffman, D., Lowenstein, H., Marsh, D.G., Platts-Mills, T.A.E., and Thomas, W. of the World Health Organization /International Union of Immunological Societies). Originally published in the Bulletin of the World Health Organization. 72(5): 796-806. Access online at http://www.allergen.org

Whyatt, R.M., Camann, D.E., Kinney, P.L., Reyes, A., Ramirez, J., Dietrich, J., Diaz, D., Holmes, D., and Perera, F.P. 2002. Residential pesticide use during pregnancy among a cohort of urban minority women. Environmental Health Perspectives. 110(5):507-514.

Wood, R.A., Flanagan, E., Van Natta, M., Chen, P.H., and Eggleston, P.A. 1998. A placebocontrolled trial of a HEPA air cleaner in the treatment of cat allergy. American Journal of Respiratory and Critical Care Medicine. 158:115-120.

Wood, R.A., Eggleston, P.A., Rand, C., Nixon, W.J., and Kanchanaraksa, S. 2001. Cockroach allergen abatement with extermination and sodium hypochlorite cleaning in inner-city homes. Annals of Allergy, Asthma, & Immunology. 87(1):60-4.

Woodcock, A., Forster, L., Matthews, E., Martin, J., Letley, L., Vickers, M., Britton, J., Strachan, D., Howarth, P., Altmann, D., Frost, C., and Custovic A. 2003. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. New England Journal of Medicine. 349: 225-36.

Appendix A. Additional Internet Resources

In addition to the references and links appearing in the reference list above, the following table provides selected links with additional information on asthma and related healthy homes issues.

Sponsoring Organization/Topic	Internet Web Site Address
Aerotech Laboratories, Inc. (Indoor air quality testing)	http://www.aerotechlabs.com/
Air Quality Sciences	http://www.aqs.com/
Allergy, Asthma & Immunology Online	http://www.allergy.mcg.edu/
Allergy and Asthma Network - Mothers of Asthmatics, Inc	http://www.aanma.org/
American Academy of Allergy, Asthma and Immunology	http://www.aaaai.org/
American Conference of Governmental Industrial Hygienists	http://www.acgih.org/home.htm
American Indoor Air Quality Council	http://www.iagcouncil.org/
American Industrial Hygiene Association (AIHA) Environmental	http://www.aiha.org/LaboratoryServices/html/empat1.htm
Microbiology Proficiency Analytical Testing (EMPAT) Program	
American Lung Association	http://www.lungusa.org
American Society of Heating, Refrigerating and Air-Conditioning	http://www.ashrae.org/
Engineers, Inc.	<u>nap.n.m.doindoiorgr</u>
Assessment Guide for Building Owners (EPA and NIOSH)	http://www.cdc.gov/niosh/bagtoc.html
Asthma and Allergy Foundation of America	http://www.aafa.org/
California Department of Health Services Indoor Air Quality Program	http://www.cal-iag.org/
Canada Mortgage and Housing Corporation (Healthy Housing &	http://www.cmhc-schl.gc.ca/en/index.cfm (http://www.cmhc-
Sustainability Project Information))	schl.gc.ca/en/imguaf/hehosu/index.cfm)
Canada Mortgage and Housing Corporation (Publications on dealing	http://www.cmhc-schl.gc.ca/en/imguaf/hehosu/hehosu_002.cfm
with moisture and eliminating the mold that can result)	
Center's for Disease Control and Prevention (CDC)	http://www.cdc.gov/
CDC's publications related to various types of mold	http://www.cdc.gov/nceh/airpollution/mold/default.htm
Center's for Disease Control and Prevention (CDC) Air Pollution and	http://www.cdc.gov/nceh/airpollution/default.htm
Respiratory Health Branch	
Children's Environmental Health Network	http://www.cehn.org/
DHHS Agency for Toxic Substances and Disease Registry	http://www.atsdr.cdc.gov/
DHHS Agency for Healthcare Research and Quality	http://www.ahrq.gov/
Environmental Health Watch	http://www.ehw.org/
Environmental Microbiology Laboratory, Inc.	http://www.emlab.com/
Health House Project of the American Lung Association	http://www.healthhouse.org/
Healthy Homes Partnership - USDA and HUD	http://www.uwex.edu/healthyhome/
HUD's Healthy Homes for Healthy Children	http://www.hud.gov/consumer/hhhchild.cfm
HUD's Office of Healthy Homes and Lead Hazard Control	http://www.hud.gov/offices/lead/
IBT Reference Lab	http://www.ibtreflab.com/
Indoor Air Pollution: An Introduction for Health Professionals (USEPA)	http://www.epa.gov/iedweb00/pubs/hpguide.html
Indoor Biotechnologies, ltd.	http://www.inbio.com/
Institute of Inspection Cleaning & Restoration (fire and flood restoration)	http://www.iicrc.org/
International Union of Immunological Societies / Allergen Nomenclature	http://www.allergen.org
Sub-Committee	
Johns Hopkins Asthma & Allergy	http://www.hopkins-allergy.org/
Master Home Environmentalist	http://www.alaw.org/air_quality/master_home_environmentalist/
Medscape's Allergy & Clinical Immunology Online	http://www.medscape.com/allergy-immunologyhome
Minnesota Department of Health Children's Environmental Health	http://www.health.state.mn.us/divs/eh/children/index.html
Minnesota Department of Health - Mold in Homes	http://www.health.state.mn.us/divs/eh/indoorair/mold/index.html
National Lung Health Education Program (NHLEP)	http://www.NLHEP.org/
National Safety Council Indoor Air Program of the Environmental Health	http://www.nsc.org/ehc/indoor/iaq.htm
Center	
New York City Department of Health (Guidelines on Assessment and	http://www.ci.nyc.ny.us/html/doh/html/epi/moldrpt1.html
Remediation of Fungi in Indoor Environments).	http://www.picid.pib.gov/dofoult.htm
NIH National Institute of Allergy and Infectious Diseases	http://www.niaid.nih.gov/default.htm

Sponsoring Organization/Topic	Internet Web Site Address
NIH National Heart, Lung, and Blood Institute	http://www.nhlbi.nih.gov/
NIH National Institute of Environmental Health Sciences Asthma	http://www.niehs.nih.gov/airborne/home.htm
Homepage	
North Carolina State University Extension Service, Mold, dust mites,	http://www.ces.ncsu.edu/depts/fcs/housing/pubs/fcs3605.html
fungi, spores, and pollen: Bioaerosols in the human environment	
Pure Air Control Services, Inc.	http://www.pureaircontrols.com/
Safer Child, Inc. – Indoor Air Pollution	http://www.saferchild.org/indoor.htm
STL P & K Microbiology (Environmental Microbiology and Mycology)	http://www.stl-inc.com/Labs/P&K/Contacts.htm
University of California Indoor Air Quality Tools: Education, Prevention	http://ehs.ucdavis.edu/ftpd/ucih/iaqtools.pdf
and Investigation	
University of Minnesota, Department of Environmental Health and	http://www.dehs.umn.edu/iaq/fungus/
Safety, Fungi in Buildings	
University of Montana Healthy Indoor Air	http://www.montana.edu/wwwcxair/
USEPA Indoor Air Quality Homepage	http://www.epa.gov/iag/
USEPA Mold Resources	http://www.epa.gov/iaq/molds/moldresources.html
USEPA Office of Children's Health Protection	http://yosemite.epa.gov/ochp/ochpweb.nsf/homepage
USEPA Mold Remediation in Schools and Commercial Buildings	http://www.epa.gov/iag/molds/mold_remediation.html