SUPPLEMENTAL MATERIAL, APPENDIX A
Critical Issues in Vulnerability in Cumulative Risk Assessment

Human and Ecological Risk Assessment

EPA makes several important distinctions in the practice of risk assessment for human and ecological endpoints generally, evident in a comparison of the frameworks for the two types of assessments (NRC 1983, U.S. EPA 1992). One of the greatest differences between risk assessments for ecological and human health protection is the level of organization at which the assessment is conducted. EPA protects humans at the level of the individual (or groups of individuals) and protects ecological endpoints at the level of the population, except for rare and endangered species protected under the Endangered Species Act. Two consequences of these approaches are that a community of people is not protected as a distinct unit, and individual (non-human) animals are not protected. As a result, a specific human community may deteriorate or disappear without raising EPA's regulatory concerns. Ecologically, a population of individual unhealthy fish is not a problem if the fish are able to survive to reproduce and sustain a population. This difference in approach has a great impact on efforts to create a common approach to assessing cumulative risk.

Human groups behave very differently from ecological groups, mainly because each type of group must deal with different limitations and stressors. Humans have a practically unlimited range because of technology – large cities have been well established in even the most hostile of environments. Ecological groups are quite different, and even a change of one degree Celsius in temperature can be catastrophic for some species. Similar differences can be found in phenomena that are shared between the two types of groups, such as immigration and emigration. Traditional definitions also differ between the two groups. Human communities are composed entirely of one species, while ecological communities are complex entities composed of many species, all interacting in some fashion. These differences will be discussed at greater depth later in this paper, but as a result of those differences, some definitions are different between the two groups.

Comparing Preparedness with Recovery

These two terms are both underlying explanations of vulnerability – they explain why or how vulnerability can happen. However, there are subtle differences between the two that are important to distinguish. Differential preparedness includes actions or efforts by the organism or community prior to risk exposure that can help soften the adverse impact of the risk when it subsequently occurs. Differential recovery refers to the function or nature of the organism or community response after the risk or exposure has been encountered. The impact of the risk factor is not reduced, rather how one recovers from the impact is affected. Preparedness can affect recovery as well. When individuals or communities are ill prepared to deal with stressors, they generally will require longer recovery times that include increased risks to the affected individuals or groups.

The distinction between vulnerability due to the ability to respond and vulnerability due to the ability to recover is somewhat artificial. Based on the information available, these factors

are mostly the same ones for individuals or groups of either people or other animals. A person or animal with a weak immune system is likely to have both a weakened defensive response to a stressor as well as a slower and less effective recovery from that stress. Therefore, unless otherwise indicated, the two types of characteristics of vulnerability will be considered together in this paper.

Interactions Among Stressors

In most cases, increasing one type of vulnerability has the overall result of increasing overall vulnerability. This increase is frequently greater than what would be expected from adjusting for one particular factor. The reason is that increases in some areas of risk can cause a domino effect, increasing the vulnerability presented from other factors. On rare occasions, increasing vulnerability in one area may actually decrease it in others. This is not the normal series of events but still occurs (U.S. EPA 2003a). It is therefore essential to examine factors affecting vulnerability in the entire context of the situation to account for the fact that overall vulnerability rarely equals the sum of its parts.

Exposure Properties

Exposure is the interaction between the receptor and the environment. To identify vulnerable receptors and assess risks from cumulative exposure, the following need to be characterized:

-Number and type of stressors (physical, biological, chemical, psychosocial),
-Spatial and temporal patterns of exposure,
-Effect of stressors on physical environment (i.e., changes in environmental conditions or habitat quality; e.g., climate change),
-Potential for stressor interactions, and
-Impact of exposures on vulnerability of receptor to impacts of subsequent exposures.

Several of these topics are covered in the companion papers (Menzie et al. 2006; Sexton and Hattis 2006). Because the emphasis in this paper is on vulnerability factors and psychosocial stressors, it will focus on relevant vulnerability factors identified under the first two categories.

As the applications for risk assessment become more complex, limitations in the source-to-effect model become apparent. Exposure assessments that are conducted using a source-to-effect model are based on the characteristics of the specific source of the exposure. As a result, the person or population modeled consists only of those persons who receive a dose from the specific source being modeled. When an assessment is required to address the total exposure to multiple stressors, there is a need to consistently identify characteristics of the receptor, and the stressors that apply to any given receptor. A receptor-oriented exposure assessment is based on the characteristics of the receptor of interest. This receptor-oriented approach is particularly important when considering vulnerability factors associated with non-chemical and psychosocial stressors. In Figure 1, the receptor is depicted at the individual, community, and population level. Both human and ecological receptors may be characterized using this model.

An important aspect of this conceptual model is the feedback, interaction, and overlap among the model components. Dashed lines around the environmental component and the receptor component indicate the dynamic and fluid nature of these entities. Depending on the particular risk question, a community may be the receptor, or the community may be the environment of an individual or population-level receptor. Two-way arrows indicate the complex interactions between environment and receptor as well as the impact of an outcome on the subsequent vulnerability of a receptor. The element of temporal and spatial patterns associated with characteristics of the model components and the interaction of these is important for application of this model, but is not depicted.

Under this conceptual model, vulnerability factors have been categorized as characteristics of the receptor or environment that alter the relationship between the receptor and environment or stress-response function. These vulnerability factors are shown in red in Figure 1. Once again, the open and dynamic nature of this system is highlighted in the overlap of many vulnerability factors across the three general categories (e.g., SES is a social factor associated with the receptor as well as a resource associated with the social environment). This overlap is also depicted in the conceptual model. Under each general category that is presented are examples of more specific factors. Many of these factors are yet again functions of many individual factors. Relevant factors may vary based on organization level of the receptor and on whether we are considering a human or ecological receptor. Here we attempt to generalize across all of these factors. This list does not address specifically all significant individual-level, community-level, and population-level metrics; these will be considered in more detail in the following sections.

The research literature directly addressing the issue of vulnerability in cumulative risk assessments is rather sparse. The authors of this paper drew on a diverse literature from the fields of public health, sociology, psychology, ecology and environmental health that directly considers the subject, and on other research and information that examines the topics included with this chapter. The examples and literature are limited to that information or research which can be applied to vulnerability in cumulative risk, not just that work which was intended to directly address these issues. The discussion examines mostly intrinsic properties of the individual or group, and those extrinsic properties (environmental) that were essential to vulnerability that we could not separate from the (mostly) group properties.

Differential Exposure, Stressors and Differential Ability to Recover

The socioeconomic stratification of American society is mirrored by health disparities for key health outcomes. Disparities in environmental exposures probably play an important, albeit poorly understood role in the origins and persistence of health disparities by race and socioeconomic status. Research on race and class differences in exposures to environmental hazards varies widely, ranging from anecdotal and descriptive studies, to rigorous statistical modeling that quantifies the extent to which race and/or SES explain disparities in environmental hazard exposures among diverse communities. Environmental health and exposure measurements in these studies include estimates of proximity to emissions sources such as hazardous waste and large industrial facilities (Boer et al. 1997; Bullard 1983; Burke 1993;

Commission for Racial Justice 1987; Hersh 1995; Mohai and Bryant 1992; Pastor et al. 2001; Pollock and Vittas 1995; Pulido et al. 1996; Sadd et al. 1999) exposure to specific substances such as pesticides and lead (Kraft and Scheberle 1995; Moses et al. 1993), exposures to outdoor air pollution and associated health risks (Gelobter 1992, 1993; Morello-Frosch et al. 2001) differences in regulatory enforcement (e.g. Superfund clean-ups) (Hird 1993; Lavelle and Coyle 1992; Zimmerman 1993), and body burden measurements (Centers for Disease Control and Prevention 2003). Although by no means unequivocal, much of the evidence points to a pattern of disproportionate exposures to toxic chemicals and associated health risks among communities of color and the poor, with racial differences often persisting across economic strata.

The specific nature of these population-based differences in exposures and how they shape health risks among diverse communities play out differently depending on other key factors and contexts, including the timing of when exposures occur during the life course (e.g., during the prenatal years, infancy, adolescence, or adulthood), whether these exposures are chronic, low level, and cumulative (e.g., through food sources, such as contaminated fish or drinking water, lead in contaminated housing, or living in areas with high levels of air pollution), or acute and sporadic (e.g. radiation exposure during pregnancy). Other factors, such as cultural practices related to diet (such as high reliance on fish consumption which may increase exposure to certain persistent bioaccumulative and toxic substances (PBTs), or gender issues that play out in the workplace (such as the lack of childcare for agricultural workers that force families, mostly mothers, to take their children to the fields thereby increasing children's exposures to pesticides). These socioeconomic, cultural, and gender dynamics can coalesce in ways that enhance population-level differences in exposures.

The Institute of Medicine has examined the research and policy issues raised by addressing the impact of environmental inequality on community health, particularly the challenge of causally linking the presence of environmental pollution with potentially adverse health effects, specifically in situations in which diverse populations are chronically exposed to complex chemical mixtures (Institute of Medicine 1999). The other methodological challenge is how to operationalize concepts of racial and socioeconomic inequality and discrimination into assessments of community hazards, exposures, outcomes, and susceptibility to the adverse health effects of environmental pollutants.

Community advocates and public health researchers and practitioners continue to debate what it is about socioeconomic inequality and discrimination that degrades the health status of those living in hazardous physical and social environments and ultimately leads to health disparities among communities of color and the poor. It is hypothesized that the collective toll of environmental (e.g., chemical agents to which communities are exposed through various media) and socioeconomic factors (e.g., material deprivation, low SES, and weak support networks) lead to health disparities among communities of color and the poor (see, for example, Gee and Payne-Sturges 2004).

Psychosocial Stress

The direct effect of hazardous social and physical environments can combine with various forms of psycho-social stress, as displayed in the central circle of Figure 1. The resulting

stress combination further widens health disparities along racial and socioeconomic lines by enhancing community exposures to toxic substances and potentially their susceptibility to the harmful effects of these exposures. The notion of susceptibility/vulnerability can emphasize independent factors that enhance the adverse effect of environmental hazard exposures, such as (but not limited to), high levels of psychosocial stress, pre-existing health conditions such as asthma, heart disease or other chronic diseases, and lack of access to resources such as healthcare. Another aspect of susceptibility is that previous hazard exposures can enhance current vulnerability to the toxic effects of pollutants, particularly if the body's defense mechanisms, ability to recover, or capacity to detoxify have already been saturated or weakened through prior exposures (see Sexton and Hattis 2006). In this regard, wildlife and other non-human receptors respond as described for people, with more adverse outcomes than anticipated.

Figure 1 conceptually demonstrates how various stressors affect groups and individual-level receptors and shape patterns of differential exposure to environmental hazards and differential ability to recover. Groups of people or animals, such as populations or communities, are largely aggregates of individuals, except in cases where the stress affects the properties of the group that are not held by an individual. The graphic uses a variation of the exposure-health outcome or source-effect continuum (from left to right). The model includes the release of an agent from a source (e.g. an indoor source such as smoking or an outdoor source such as an industrial facility) through exposure via various media (such as air) and the occurrence of a health effect (e.g. an adverse outcome such as low birth weight).

This framework implies that the emission or presence of an environmental agent must first lead to exposure and overcome the individual's or communities' defense systems in order to have an adverse effect. For example, environmental tobacco smoke (ETS) has a complex mixture of over 4000 chemicals, including polycylic aromatic hydrocarbons (PAH) and carbon monoxide (Centers for Disease Control 2000; Lewtas 1994), where a smoker in the home emits pollutants that achieve a certain concentration where exposure via breathing contaminated air leads to an internal dose. The internal dose may have no health effect until it achieves a biologically effective dose, depending on the extent of accumulation, biotransformation, and elimination in the body. The same is true for other complex releases into air or water (storm sewers, incinerator emissions), and for animals other than people. The dose, if not effectively metabolized by the body's detoxifying and/or immune systems, can lead to biological effects that may alter system functioning and lead to adverse health outcomes (e.g. low birth weight). Individual and community-level stressors shape how these differential exposures play out, including increasing or decreasing absorption, ability to detoxify or recover, and the ultimate health effect from environmental toxins. A comparable consideration for an ecological system would be the exposure of fish to the discharge from a storm water sewer that contains lead, copper, sediment, and bacteria. The fish may accumulate the lead and copper without any apparent effect until some internal level at which reproduction, neurological function, etc. begin to fail or suffer adverse effects. However, this model does not consider the possibility that the mere presence of the source of a stressor presents a non-physiological, psychological reaction in individuals or communities.

Stressors can enhance vulnerability as shown in Figure 1, and can be conceptualized to cover both biological and non-biological factors, including genetic predisposition, pre-existing

health conditions, social conditions, and psychosocial stress. All of these indicators of vulnerability can be measured at the individual and/or community or population level along the exposure-health outcome continuum.

A full assessment of potential stressors and how they amplify vulnerability along the exposure-outcome continuum are not well understood, particularly for psychosocial stress. Given that stress may possibly induce a latent effect of a toxicant, there is the possibility that chronic stress could alter basic physiological functions or development, such as *in utero* development, and shift the threshold for potentially adverse birth outcomes such as low birth weight, neurotoxicity and other effects. Interestingly, there is no basic difference between humans and non-human animals in this aspect of the assessment conceptual model. Some research on the adverse effects of ETS on offspring offers insight. For example, Sadler and Belanger et al. (1999) showed that prenatal ETS exposure was associated with small size for gestational age only for low income women and not for the higher income groups. Similarly, Rauh et al. (2004) showed that prenatal exposure to ETS in the home has a negative effect on 2-year cognitive development, and that this effect is exacerbated under conditions of maternal hardship.

Although these studies suggest that psychosocial stress may alter the toxic effects of pollutant exposures such as ETS, the biological mechanism of this effect remains unclear. Nevertheless, the importance of considering the joint effects of chemical agents including ETS with other prenatal exposures to stressors and buffers, rather than simply controlling for individual and community-level factors, appears to be warranted. Furthermore, it is possible that psychosocial stress may be indicators for exposures to other unmeasured toxicants so that the apparent interaction observed in some environmental health studies merely reflects a synergistic impact with other pollutants such as pesticides, volatile organic compounds and other unmeasured ambient air pollutants (Whyatt et al. 2002). Nevertheless, stress may have its own unique biological impact, both in terms of amplifying differential vulnerability to the toxic effects of pollutants or by weakening the ability to recover from harmful exposures. In terms of ability to recover, the body's biotransformation or detoxification systems can remove or effectively metabolize these toxins, yet under conditions of chronic stress, these defense systems may be impaired and result in compromised organ resistance to the effects of an environmental toxin. Again, there is no difference between humans and wildlife at this stage. In addition, stress itself may lead directly to illness, which in turn, renders the individual more susceptible to the toxic effects. Illness may also compromise the capacity to cope and recover from adverse environmental exposures (Rios et al. 1993). Furthermore, the literature suggests that individual and community level stressors can differentially moderate exposure-outcome relationships. Therefore, it is important to examine both levels of stressors to assess their impact on health outcomes that are both environmentally and socially mediated (Diez-Roux 1997, 1998, 2000; Rauh et al. 2004).

The model indicates that the properties of individuals, communities, and populations may interact to form distinct outcomes where vulnerabilities influence both the nature of stressors as well as the outcomes and is discussed below. This paper elaborates on and argues that deterioration of resources or intervention tools will substantially degrade the ability to respond and recover and will further diminish resources.

Supplemental Material, Appendix B, Case Studies in Vulnerability in Cumulative Risk Assessment

A. Community-Level and Individual-Level Dimensions that Affect Childhood Asthma Morbidity- Implications for Risk Assessment

Human health and disease occur in biological, environmental, socioeconomic, and psychosocial contexts. These contexts include area-level factors that encompass the economic, environmental, educational, housing, public health/medical and other community dimensions (Hillemeier et al. 2003) as well as related individual-level factors, such as SES, race (or experience with racial discrimination), diet, genetics, and health behaviors, among others (Klinnert et al. 2002). Childhood asthma exemplifies how inextricably linked these individual and community-level dimensions can be in terms of how they affect morbidity, incidence and severity of disease. As one of the most common chronic childhood disease in the United States, asthma disproportionately affects many socioeconomically disadvantaged urban communities, as demonstrated in Figure 1 (U.S. EPA 2003b).

Asthma prevalence, hospitalization, and mortality are higher for African American compared to white children (Institute of Medicine 2000). Access to competent, preventive health care is well known to have a significant influence on asthma hospitalizations and mortality, as effective asthma management protocols greatly reduce the need for hospitalization and should eliminate mortality. Research suggests that even within prosperous middle class communities, unmeasured socioeconomic stressors (such as racial discrimination, differential access to health care, housing segregation) may contribute to these persistent race-based disparities (Nelson et al. 1997; O'Neill et al. 2003).

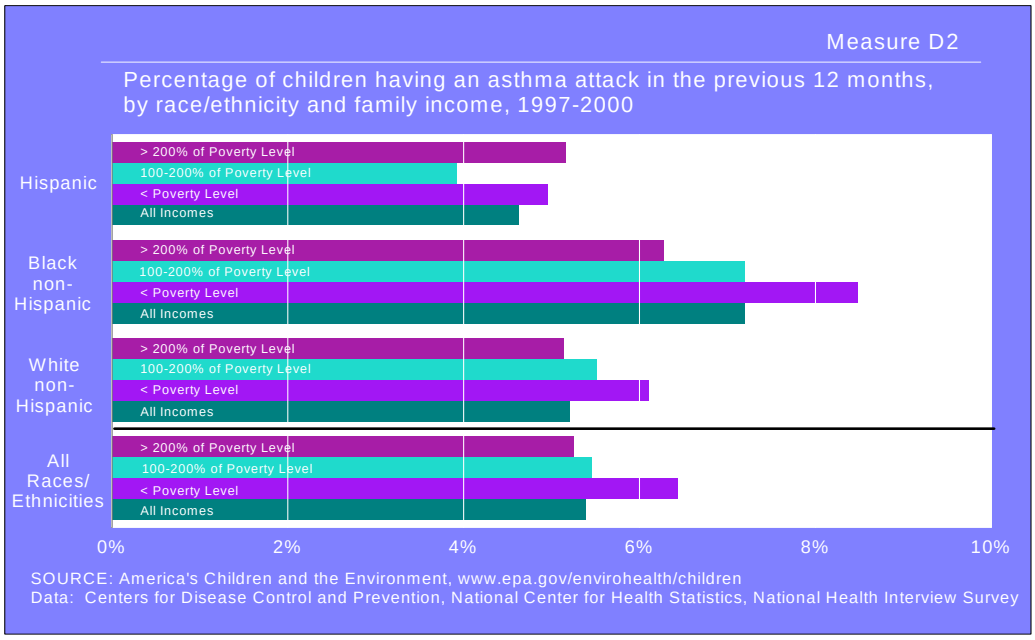

Figure 1 (taken from US EPA 2003b). Prevalence of asthma in children as a function of socio-economic status and race in the US.

Research has sought to assess whether racial disparities in asthma can be explained by urban residence or by factors related to socioeconomic status. Using data form four U.S. cities, black children were 1.6 times as likely to have an asthma diagnosis compared to white children, even after taking into account exposures such as cigarette smoke, body-mass index, use of air conditioning, city of residence, parental respiratory illness, parental education, only child status, and single parent household (Gold et al. 1993).

There is a growing body of research on the adverse health effects of air pollution on children's respiratory health, and most of this work relates specifically to criteria pollutants. For many years, scientists distinguished between exacerbation of existing asthma and factors that cause asthma because of the argument that outdoor air pollutants may aggravate existing asthma, but may not directly cause the development of the disease (Koenig 1999). However, recent research has challenged this assumption by linking ozone exposure with the development of asthma among young children who play outdoor sports (McConnell et al. 2002). Other work suggests that children are particularly vulnerable to early effects of pollution exposure and that early changes in lung development may not be effectively reversible.

It is clear that traditional environmental factors alone do not fully explain asthma, owing to the genetic component. New research emphasis has begun to examine ways in which stressors at the individual and community levels may influence the development and severity of childhood asthma and impact diverse populations in myriad and complex ways (Busse et al. 1995; House et al. 1988; Wright et al. 1998). Although no clear causal link between psychosocial stress and childhood asthma has been established and the relationships between indoor and outdoor environmental factors and asthma onset are still being determined, risk assessment approaches need to consider ways in which community- and individual-level factors can act as potential mediators of relationships between environmental pollutant exposure and asthma.

Relatively little research has examined the effect of community-level social variables on asthma, although recent studies suggest a relationship between increased neighborhood income inequality and higher childhood asthma hospitalization rates (Gold and Wright 2005). Gold and Wright suggest three plausible pathways that link community and individual-level influences to asthma morbidity: 1) differential environmental exposures, 2) psychosocial stress and 3) the impact of 1 and 2 on individual health behaviors (Gold and Wright 2005).

Although research and risk assessment have emphasized the proximate physical and environmental factors associated with childhood asthma, there has been no research that has examined the socioeconomic and political drivers that segregate certain populations in disadvantaged neighborhoods and lead to disparities in exposures to environmental risk factors in ways that may explain disparities in disease rates. Residential segregation by race and to a lesser extent class, can be viewed as a potential driver of differential exposures to environmental hazards, poverty, and neighborhood level stressors that may be linked to adverse health outcomes such as childhood asthma (Morello-Frosch 2002). In addition to environmental factors, chronic life stress experiences may also affect childhood asthma morbidity. Recent studies indicate that higher levels of caregiver stress (Wright et al. 2002) as well as exposure to

community level violence (Wright et al. 2004) are associated with more severe asthma morbidity.

Disparities in exposures to environmental hazards as well as chronic stressors can shape individual-level factors and behaviors that are associated with childhood asthma. For example, tobacco smoke exposure is an important factor associated with the occurrence of childhood asthma (Li et al. 2005; Strachan and Cook 1998), and smoking prevalence is often associated with chronic stress and the targeted marketing of tobacco products in poor communities of color (Pollay et al. 1992). The impact of stress on smoking behavior can occur at both the community and individual level (Kleinschmidt et al. 1997). Similarly, community food security impacts access to affordable supermarkets, which can affect an individual's dietary intake of fresh fruits and vegetables. A significant body of evidence indicates that diet and nutritional status impacts respiratory health in children (Gilliland et al. 2003). It is hypothesized that certain vitamins found in fruits and vegetables may protect the lungs against oxidative stress and promote healthy lung function and development (Gilliland et al. 2003).

Figure 2 proposes one possible scenario of how community-level and individual-level factors can combine in ways that contribute directly to childhood asthma morbidity and the incidence and prevalence of disease. These factors can also enhance community-level and individual-level vulnerability to the toxic effects of pollutant exposures. Drawing upon previous work (Gilliland et al. 1999), the figure suggests important areas for understanding the complex relationships between community-level and individual-level dimensions that could be considered quantitatively or qualitatively in the context of environmental health risk assessment.

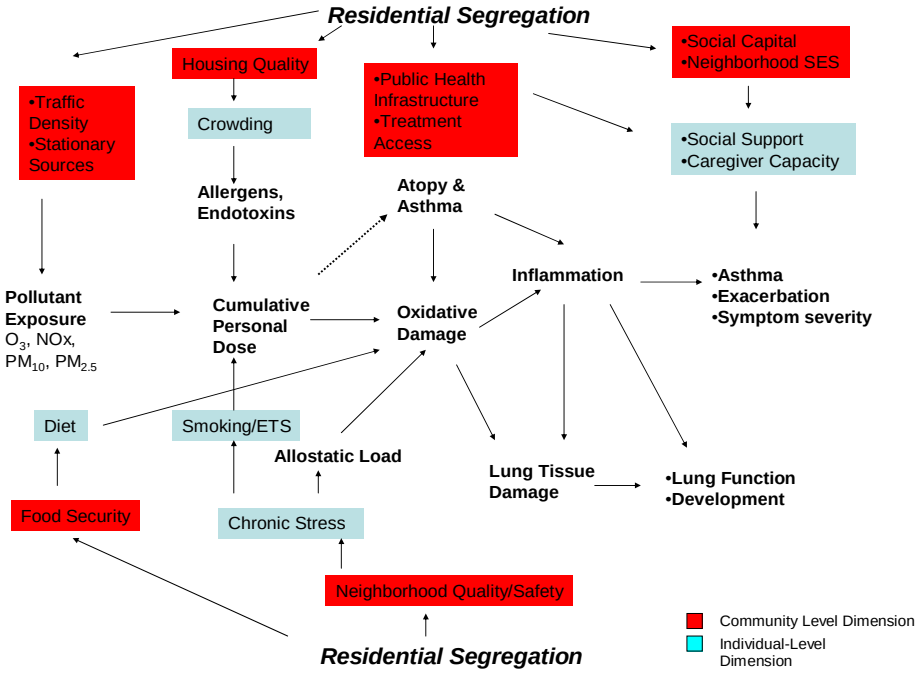

Figure 2: Community-level and individual-level factors that impact the pathway linking pollutant exposures and childhood asthma

The factors considered in this figure are by no means exhaustive, but are based on the brief literature review described above and are used to show how these complex, multi-level relationships can play out. The model assumes that residential segregation plays an overarching role in shaping the primary sources of air pollution exposure as well as the community-level factors that can directly or indirectly shape the complex pathways linking pollutants with asthma development and morbidity. Each of these community-level dimensions can act as stressors or buffers that impact individual-level vulnerability that may be associated with childhood asthma, including health behaviors (smoking and diet), caregiver capacity, household conditions (such as crowding) and chronic stress. All of these factors can influence the biological pathways linking pollutant exposures to asthma exacerbation and possibly the development of disease. The dotted arrow is meant to highlight the fact that although existing research has elucidated what factors aggravate existing asthma, it tells us little about those factors linked to asthma development in children.

B. Coastal and Estuarine Low Oxygen as Cumulative Risk

Depletion of oxygen dissolved in water is one of the most significant threats to coastal ecosystems. This condition, known as hypoxia (literally low oxygen) can lead to complete absence of oxygen, anoxia, under extreme conditions. Technically, any depletion of oxygen below a condition of full saturation is hypoxia, but for practical purposes, scientists and managers acknowledge that normal fluctuations cause oxygen to decline somewhat, i.e. 20%. Hypoxia is a problem when dissolved oxygen in water falls below the level necessary for the survival of animals and plants living in that water body (see Rabalais and Turner 2001). Persistent areas of hypoxia have been documented in the Gulf of Mexico, the Chesapeake Bay, Long Island Sound, and a number of other costal regions in the United States and around the world (Diaz and Rosenberg 1995; Rabalais and Turner 2001; Roman et al 1993). The duration, area and length of hypoxia events is variable, in some cases lasting for months and covering an area as large as the state of New Jersey at the mouth of the Mississippi River in the Gulf of Mexico. Hypoxia events are growing more common across the world, and can lead to a variety of secondary effects such as elevated carbon dioxide levels and severe drops in pH (NRC 2000).

Hypoxic conditions generally arise as a result of a phenomenon known as eutrophication, an increase in nutrient input that causes rapid and unsustainable growth of living systems (Paerl 1995, 1997). When water bodies receive excess nutrients (i.e. phosphates and nitrates), a chain reaction can begin where single cell algae growth fed by nutrients begins to spiral out of control. The increase in algae also stimulates the growth of microscopic animals (zooplankton) that feed on the algae. Eventually, the algal growth becomes so dense that it significantly reduces the area of the water column where photosynthetic activity can occur. The algal and zooplankton growth cannot be sustained and eventually the nutrients are exhausted, leaving the algae without enough food, and the algal population dies, followed by the zooplankton population (Figure 3). As plant matter and then animals begin to die off, bacteria that decompose dead tissues thrive and oxygen levels decline. The dead tissue results in a tremendous increase in the amount of waste and detritus in the system, see Rabalais and Turner (2001). This waste feeds the population of heterotrophic bacteria that breakdown dead and decaying material. The metabolism of the

bacteria consumes oxygen, produces carbon dioxide and removes significant amounts of oxygen from the system.

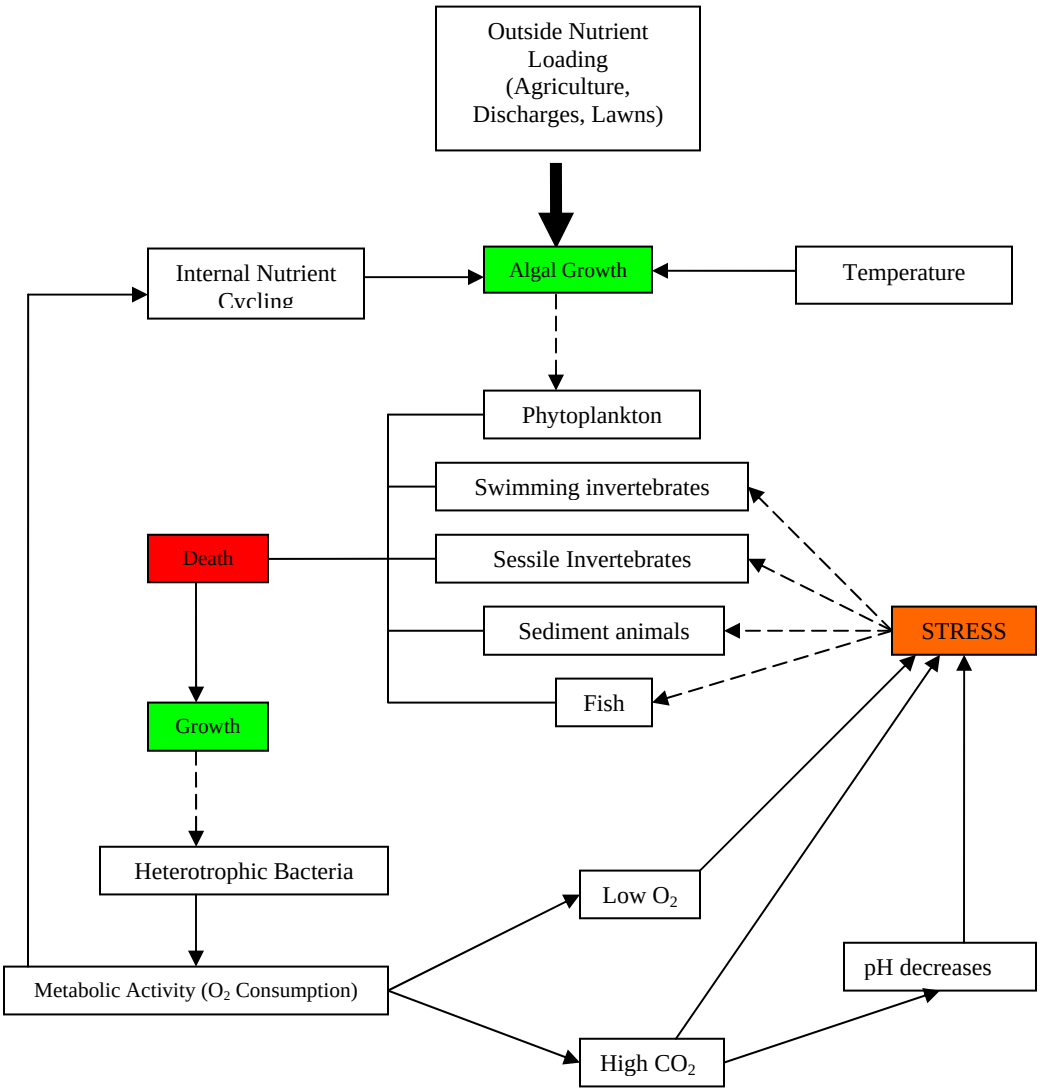

Figure 3. Conceptual model of low oxygen (hypoxia) in coastal waters. Nutrients (nitrogen and phosphorous compounds) from land-based sources drive an uncontrolled growth of algae. The larger algal population cannot be sustained, dies, decomposes and the bacterial population consumes so much oxygen that oxygen dissolved in the water declines dramatically.

Under eutrophic conditions in the Gulf of Mexico, bacteria within sediment (the most significant detritivores in aquatic systems) have been found to account for roughly 20-30% of total oxygen depletion (Bierman et al. 1994). Hypoxia is more common when eutrofication occurs where the water column is stratified due to differences in either salinity or temperature (Stow et al. 2005). Such stratification prevents mixing of fresh, oxygenated surface water, and dense, high salinity hypoxic water on the bottom.

Eutrophication can cause or contribute to other harmful conditions that are associated with but are directly caused by hypoxia. The accelerated rate of decomposition present under eutrophic conditions greatly increases both oxygen consumption and carbon dioxide (CO_2) production. Increasing CO_2 production caused by heterotrophic bacteria increases dissolved CO_2 in the water column, a condition known as hypercapnia (Cochran and Burnett 1996). Elevated carbon dioxide may be directly toxic to organisms, and can cause other effects by altering water chemistry. Increased carbon dioxide causes water pH to decrease, despite any buffering. Thus, aquatic hypoxia is often accompanied by other environmental changes that present additional risks to aquatic organisms.

The secondary effects of eutrophication can be more harmful to organisms than the high nutrient levels associated with it (Gray et al 2002). These conditions cause more and more organisms to die, returning nutrients to the system and fueling more decomposition, which in turn continues the process and allows hypoxic conditions to persist for longer periods of time. Organisms that cannot avoid or adapt to these conditions will perish (see Burnett and Stickle 2001).

Animals have a wide variety of responses to hypoxia-induced stress. Many organisms are unable to avoid oxygen depleted waters, and use several physiological responses to mitigate the stressful conditions associated with hypoxia. For motile organisms such as fish, shrimp, crabs, etc., avoidance and increased ventilation are the most common responses (reviewed by Burnett and Stickle 2001). Animals increase production of oxygen carrying respiratory pigments such as hemoglobin or increase blood flow (Burnett and Johansen 1981; Hagerman 1986). Under chronic hypoxic conditions, vertebrates, insects, crabs and likely other animals may also alter the structure of respiratory pigments to allow for greater oxygen carrying capacity (deFur and Pease 1988; deFur et al. 1990). Physiological responses and tolerances vary by species, creating species specific dose-response curves. These responses can compensate for some adverse effects of hypoxia, but organisms are simultaneously exposed to other adverse conditions.

As noted above, hypoxia is frequently (if not always) accompanied by hypercapnia and acidified waters. Excess carbon dioxide is dangerous to organisms for a variety of reasons. High CO_2 can cause acidification of body tissues and blood, and alter physiological responses unrelated to exposure to low levels of oxygen (Boleza et al. 2001; Hayashi et al. 2004). If hypoxia is induced by eutrophication, then organisms will be exposed to other stressors such as excess nutrients, low pH, increased sediment in the water, and changes in salinity or temperature. In rare instances, upwelling of hypoxic waters containing high levels of hydrogen sulfide (a toxic byproduct of anaerobic bacteria metabolism) can cause fish kills when winds blow the toxic water into shallow areas where fish and other organisms are unable to escape (Rabalais et al. 2001). During most hypoxic events, aquatic animals will be exposed to several of these stressors in addition to low oxygen levels.

Risk assessments for waters with a significant risk of hypoxia must also consider accompanying stressors and secondary effects that are often associated with such conditions. The cleanup of the Chesapeake Bay is an excellent example of a system-wide effort that has all the characteristics of a risk assessment, described by deFur (1997). The original assessment of the Chesapeake Bay identified ten problems, ranging from excess nutrients, loss of living resources and toxic chemical contamination, to oxygen depletion and habitat degradation. The cleanup process

prioritized the top ten risks to the Bay system, recognizing that the risks are combined exposures in time and space. The Bay program listed low oxygen conditions as one of the most serious risks to the ecosystem because of the long term consequences and seriousness of the effects.

Hypoxia generally exposes organisms to multiple and diverse stressors that have responses unrelated to one another. Since each species responds differently to these stressors, some populations will be more affected than others. Microscopic organisms are the first to be affected, with larger animals affected as oxygen levels drop further. Adverse effects on functionally significant sections of an ecosystem can have a ripple effect through the rest of the community, creating additional stressors that are based on community species composition. The risks for hypoxia are therefore the cumulative effects of all conditions including low oxygen levels, hypercapnia, changes in pH, and additional effects specific to individual populations and communities.

General trends in the response of populations and communities to hypoxia have been documented, and form a distinct exposure-response curve (Figure 4, adapted from Rabalais et al. 2001; Diaz and Rosenberg 1995). Animals in the water are the first to be affected, dropping off significantly at the onset of hypoxic conditions (< 2.0 mg O_2 l^{-1}). Free-swimming and bottom-dwelling invertebrates suffer adverse effects at slightly lower oxygen levels, begin to die off at 1.5 mg O_2 l^{-1}, and are completely absent under 1.0 mg O_2 l^{-1}. Larger animals become stressed when oxygen levels drop below 1.0 mg O_2 l^{-1}, and die off under 0.5 mg O_2 l^{-1} (Adapted from Rabalais et al. 2001; Diaz and Rosenberg 1995). This relationship (Figure 4) is characteristic of initial responses to hypoxia; long term responses may vary significantly based on community composition and other factors. The overall response may also be influenced by species-specific responses to associated effects such as hypercapnia and pH change.

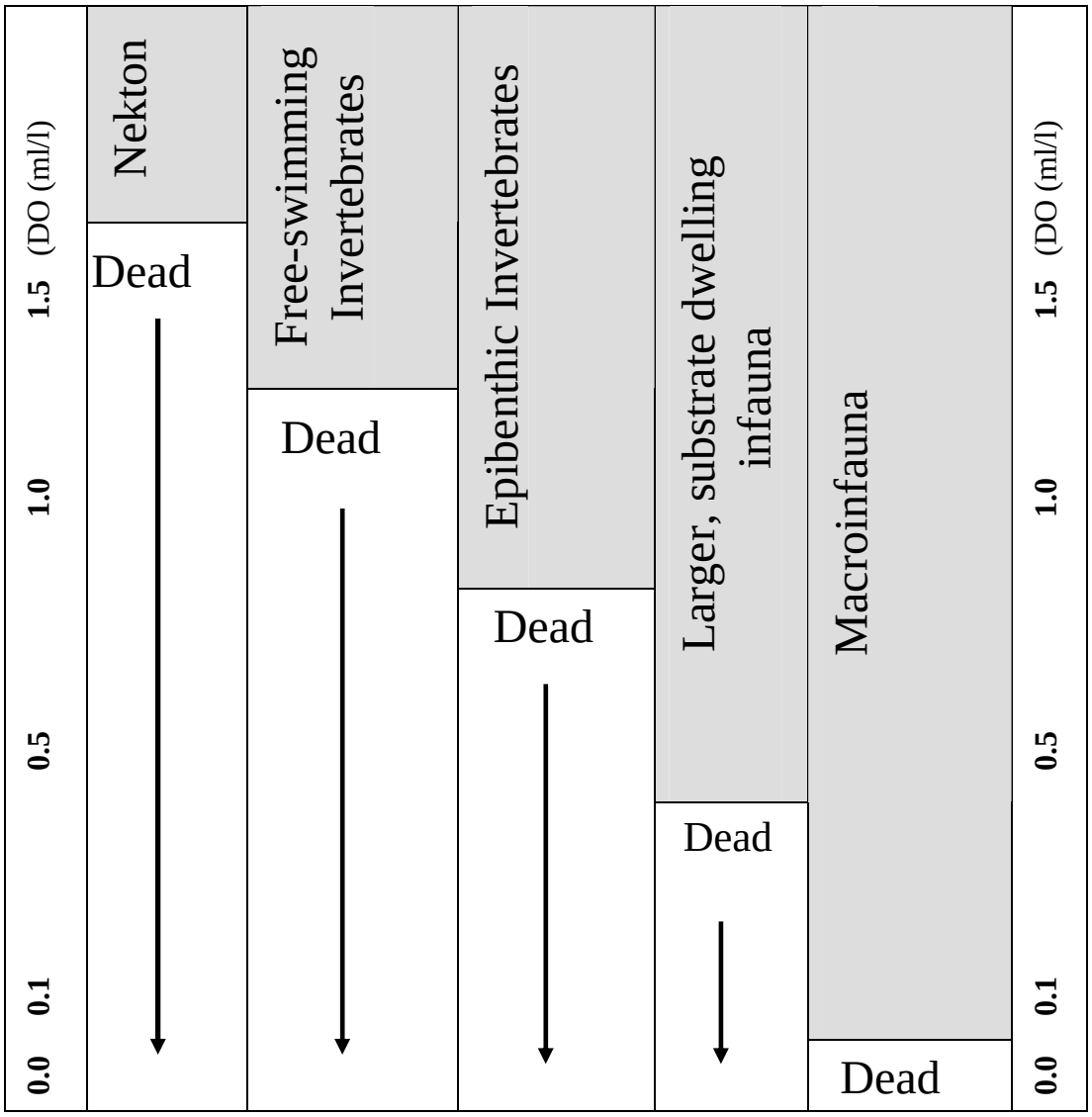

FIGURE 4: The approximate relationship between hypoxia and the survival and abundance of various groups of aquatic animals. Hypoxia is given on the Y-axis over the limited range of dissolved oxygen levels 0-1.5 ml/l (Adapted from Rabalais et al 2001; Diaz and Rosenberg 1995)

Perhaps the greatest risk from hypoxia is that some stressors associated with the phenomenon increase the overall vulnerability of exposed organisms and communities to other stressors. The higher nutrient levels that cause eutrophic-induced hypoxia, in particular nitrite can alter hemoglobin function in organisms (Das et al. 2004). Hypercapnia can drastically reduce the efficiency of oxygen transport, as well as causing other adverse effects (Crocker and Cech Jr. 1998). These two stressors compound the responses to low oxygen levels, thereby intensifying risk. The interactions of these stressors create a scenario where actual risks are greater than the sum of responses to the individual stressors encountered. Excess sediment in the water will clog the gills of a fish, clam or crab that is already struggling to obtain oxygen from hypoxic waters.

This scenario illustrates the difficulty of including issues regarding vulnerability into a framework of cumulative risk assessment. Cumulative risk assessment is already made difficult by the need to produce a common metric for highly variable stressors (U.S. EPA 2003). The

incorporation of factors contributing to an ecological unit's ability to respond to or recover from stress requires the formation of multipliers to the metrics used in risk calculations. The additional risks posed by increased vulnerability are not additive, and instead can increase risks exponentially.

To evaluate risks in systems where multiple stressors are acting on ecosystems and their respective units, assessors must consider the interactions of the various stressors and how they may enhance or mitigate endpoints. Traditional risk assessment is limited to the separation of individual stressors and their endpoints independent of other factors that may increase the vulnerability of the system. To compensate for this, assessors should evaluate how each stressor affects the vulnerability to others that an ecological unit would be exposed to in a given scenario. Only after such an evaluation should an assessor begin to characterize the cumulative risks facing an ecological unit.

Supplemental Material, Appendix C: Methods for Measuring Levels of Vulnerability

While the relationships among all the many factors that affect individual and community response to environmental stressors are very complex and not well researched, we are able to identify factors that are likely to increase vulnerability. It will be valuable to undertake research that will more fully elucidate these relationships. In the meantime, many of the most basic vulnerability factors can be measured now, even though all the relationships cannot be quantified. These measurements include:

- age
- gender
- race/ethnicity
- socioeconomic status (or perhaps household income)
- access to health care

Larger metropolitan areas are identified by the census as standard metropolitan statistical areas. These typically reflect county boundaries. Census can be obtained by county, so if counties are useful as a unit of analysis, demographic characteristics by county can be compared. This will allow large areas that have populations with a greater prevalence of vulnerability factors to be identified.

Another approach that may be relevant in some cases is to use data sources that include information about the characteristics of the individuals included in the data source. Such an approach is typically more relevant to data about health outcomes in part because such data are collected from individuals. Measures of individual vulnerability factors include:

<u>Human Metrics:</u>

- Socioeconomic Level- Income
- Gender
- Race/ethnicity
- Age
- Health Status
    - Rates of Illness or Disease
    - Stress Levels
    - Emotionality Tests (positive/negative outlook)
    - Assays of Depression/Anxiety

- Health Care Metrics
    - Hospital Density
    - Number of Beds
    - Number of Health Professionals Employed
- Traditional Cumulative Risk measures for human health:
    - Cancer Slope
    - Environmental Exposures (smoking, chemical levels, etc.)
    - Hazard Index
    - Disease Rates

Community Metrics

- Unemployment Level and other employment metrics
- Education metrics
    - Number of Schools
    - Average Class Size
    - Density
    - Dropout Rates
- Racial residential segregation
- Income inequality
- Material deprivation and Poverty
- Wealth/Assets (e.g. home ownership)
- Other metrics that may indirectly measure other factors
    - Crime rates
    - Divorce Rates
    - Frequency and Severity of Disturbance

Methodology for Individual Level Human Vulnerability Factors:

- SES
  Research on SES indicates that household income is the primary factor influencing child developmental health (Magnuson and Duncan 2002, Mc Loyd 1998) and adult physical health (Adler et al. 1993). Household income is best measured by the income to needs ratio which equals one at the federal poverty line. This information is published annually by the census and is calculated according to family size and structure (i.e., it is a per capita, adjusted for costs of living index). The environmental justice literature suggests that race/ethnicity and SES both contribute as risk factors.
- Disease Incidence, health status and birth data
  Standard medical diagnostic protocols and some self report instruments are available for many assessments. Medical diagnoses are preferable to identify disease, but where clinical encounters are not an option, survey or self report instruments may be appropriate. Significant cost tradeoffs need to be considered when selecting the appropriate approach. Vital statistics data are universally available, including birth data, birth weight being critically important risk factor for other health conditions (Silbergeld and Tonat 1994).
- Biomonitoring data
  Data about some kinds of contaminants in human tissues may be available in some cases. Blood levels are reported in many areas and can be available for an area of interest. The national NHANES study measures some chemicals are human tissues, and some of these,

such as methyl mercury, can be interpreted as they relate to risk. Others that are measured cannot be interpreted in that way. In few cases are such data available for a particular area unless a special study has been done.

- Smoking
  Both the number and duration of smoking should be assessed. In epidemiological research this is typically constructed as number of pack years. Both smoking and second-hand smoke exposure need to be assessed, the latter may only be assessable indirectly. In some cases, survey data such as from the Behavioral Risk Factors Survey System may be available about smoking status or other risk factors.
- Psychological stress
  There are numerous psychological stress instruments. Cohen et al. (1995) provides an excellent overview of the measurement of psychological stress. One of the most commonly used and straightforward instruments of the assessment of stress is the Perceived Stress Scale (Cohen and Williamson 1988).
- Negative emotionality, negative affect
  In children this can be assessed by standard assessments of temperament. See Rothbart and Bates (1998) for a good overview of these measures. The Positive and Negative Affect Scale (PANAS) is often used to assess negative affectivity in adults (Watson and Pennebaker 1989).
- Psychological distress
  There are a large number of instruments to assess depression, anxiety, and related disorders on both children and adults. The most common instruments for children's assessment are Achenbach (1991) and Rutter et al. (1970). For adults depression is most typically indexed by the CESD (Radloff 1977) and for anxiety a common tool is the Spielberger Trait Anxiety measure (Spielberger 1970).

Methodology for Measuring Ecological Vulnerability

- Quality of Habitat
  Ecological systems require high quality habitat to maintain resilience and reduce vulnerability. Therefore, metrics associated with habitat quality include size, contaminant levels, frequency and intensity of disturbance, climate and temperature, percent edge space, and frequency and severity of disease, total organic carbon, nutrient levels, etc.
- Genetic Diversity
  Ecological populations rely heavily on genetic diversity in order to maintain themselves in the event of stressors. Genetic markers such as the frequency of alleles, micro-satellites, allosomes or isosomes can all be used to measure genetic diversity.
- Species Richness of Habitat
  More diverse habitats are less susceptible to stressors, and therefore the Shannon-Weinberg or Simpsons Indices are the most relevant metrics for this variable.
- Metrics of Keystone Species
  In many ecosystems the overall health of the system is related to the health of ecologically significant species. Population metrics for those species such as fecundity and death rates, population size, immigration and emigration, predation rates, and average lifespan are all valuable metrics when assessing a particular population of one species.

Shared Characteristics:

There are many characteristics that are common to both ecological and human systems that influence vulnerability. Potential measurements common to both groups are as follows:

- Population Density
- Geographic size of community/population/habitat
- Reproductive Rates
- Mortality Rates
- Age
- Frequency and Severity of Disturbances

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