Date: January 2, 2008

Exposure Information in Environmental Health Research:
Current Opportunities and Future Directions for Particulate Matter, Ozone, and Toxic Air Pollutants

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Running title: Exposure assessment in public health research

Abstract

Understanding and quantifying outdoor and indoor sources of human exposure are essential but often not adequately addressed in health-effects studies for air pollution. Air pollution epidemiology, risk assessment, health tracking and accountability assessments are examples of health-effects studies that require but often lack adequate exposure information. Recent advances in exposure modeling along with better information on time-activity and exposure factors data provide us with unique opportunities to improve the assignment of exposures for both future and ongoing studies linking air pollution to health impacts. In September 2006, scientists from the US Environmental Protection Agency (EPA) and the Centers for Disease Control and Prevention (CDC) along with scientists from the academic community and state health departments convened a symposium on air pollution exposure and health in order to identify, evaluate, and improve current approaches for linking air pollution exposures to disease. This manuscript presents the key issues, challenges and recommendations identified by the exposure working group, who used cases studies of particulate matter, ozone, and toxic air pollutant exposure to evaluate health-effects for air pollution. One of the over-arching lessons of this workshop is that obtaining better exposure information for these different health-effects studies requires both goal-setting for what is needed and mapping out the transition pathway from current capabilities to meeting these goals. Meeting our long-term goals requires definition of incremental steps that provide useful information for the interim and move us toward our long-term goals. Another over-arching theme among the three different pollutants and the different health study approaches is the need for integration among alternate exposure assessment approaches. For example, different groups may advocate exposure indicators, biomonitoring, mapping methods (GIS), modeling, environmental media monitoring, and/or personal exposure modeling. However, emerging research reveals that the greatest progress comes from integration among two or more of these efforts.

Introduction

Accurate assessment of human exposures is an important part of environmental-health research. Both outdoor and indoor sources of pollutants influence an individual's exposures during the course of their lives and daily activities. Understanding and quantifying these exposures are essential but they are often not adequately addressed in health-effects studies for air pollution. Air pollution epidemiology, risk assessment, health tracking and accountability assessments are examples of health-effects studies that require but often lack adequate exposure information. For example, most air pollution epidemiology studies make use of potentially unreliable surrogates of personal exposures, such as information based on available central-site outdoor concentration monitoring or modeling data. However, more explicit studies reveal that personal exposures tend to be greater in magnitude and more variable in location and time than the corresponding ambient concentrations. Examples are individuals near major point- or on-road-emission sources of air pollutants such as particulate matter [PM] and hazardous air pollutants (HAPs). Other examples are individuals exposed during their daily activities to higher levels of outdoor pollutants such as ozone or of indoor pollutants such as combustion products including nitrogen dioxide (NO_2) and semi-volatile organic compounds (SVOCs) (Spengler et al., 1994; Özkaynak et al., 2007).

Complex patterns in the spatial variation of exposures among different population cohorts, especially in the context of cross-sectional or intra-urban analysis of air pollution health effects, remains challenging. Recent research has shown that the variations in exposure-to-concentration ratios can be highly dependent on pollutant type and the locations and activities of the exposed population (Özkaynak et al., 2007, Isakov et al., 2006). Thus, the assignment of outdoor concentrations as a proxy for personal exposures introduces varying degrees of exposure misclassification. The degree of misclassification depends on the nature of the epidemiologic model tested and the statistical methodology employed. Moreover, the use of simple proxies in the assignment of exposures often have important implications for both the design and the interpretation of the findings derived from community air pollution health studies. Recent advances in exposure modeling along with better information on time-activity, commuting patterns, and exposure factors data, provide us with unique opportunities to improve the assignment of exposures for both future and ongoing studies linking air pollution to health impacts.

In September 2006, scientists from the US Environmental Protection Agency (EPA) and the Centers for Disease Control and Prevention (CDC) along with scientists from the academic community and state health departments convened a symposium on air pollution exposure and health in order to identify, evaluate, and improve current approaches for linking air pollution exposures to disease. Scientists from these different sectors worked to develop consensus on the capabilities and limitations of the current state of the science and then made recommendations and set priorities for near-term and long-term research goals that could improve this linking process. The symposium participants divided themselves into working groups that focused on the specific topics of (i) exposure, (ii) health information, (iii) emerging issues, and (iv) linking exposure and health data. This manuscript focuses on the research efforts of the first of these working groups and presents the key issues, challenges and recommendations identified by the exposure working group—referred from here on as the workgroup. In order to explore key issues and develop findings and recommendations, this workgroup used case studies of PM, ozone, and toxic-air-pollutant exposure in the context of air pollution epidemiology, risk assessment, environmental public health tracking (EPHT) or surveillance studies, and accountability. The two companion papers by Özkaynak et al. (2007) and Thurston et al (2007), which appear in this issue of the *Journal*, summarize the overall findings from this symposium and the issues and recommendations regarding health information, respectively.

Our objectives in this manuscript are to report the issues and approaches used in the September 2006 workshop to determine short-term and long-term goals to improve the use of monitoring data and exposure model results for PM, ozone, and toxic air pollution in health surveillance and health research studies. The Approach and Methods section below describes how the workshop was organized and used to select and set priorities among the issues that should be considered and the research needed to confront these issues. This section also describes how the participants in the exposure workgroup selected a set of key issues and used these issues to explore limitations, barriers, and challenges to improving health surveillance and health impacts research. As part of the methods development process, the workgroup agreed to address the following key issues:

(1) Differential Exposures—Indoor, Outdoor and Other Environments

(2) The Impact of Population Location and Mobility

(3) Biologically Relevant Time Scales

(4) Age-Specific Exposure Issues

(5) Exposures to Multiple Pollutants

(6) Tracking Effect Modifiers

(7) Tracking Exposures for Long-Latency Outcomes

(8) Tracking Exposure-Outcome over Short Time Scales

The Results section provides the workgroup's findings on each of these key issues in the context of limitations, barriers, and challenges. This is followed by a discussion of priorities for actions to understand limitations, confront challenges, and remove barriers.

Approach and Methods

Our approach to this research and the process for developing our findings includes three primary activities, all structured around the workgroup process. First, the symposium organizers described to the participants how the workgroup process would be used to explore key issues and set research priorities. Second, the symposium organizers developed the conceptual framework in which participants could identify and evaluate short-term and long-term efforts needed to confront the limitations, barriers, and challenges to linking disease and exposure. In describing this framework, we compare here classical epidemiology, risk assessment, health tracking, and accountability in order to evaluate the needs of these different health-research efforts for information relating exposure to disease. In Table 1, we define each of these terms. Finally, the organizers identified and described substances of interest that provide informative case studies for the workgroup evaluations.

The Conceptual Framework for Linking Air Pollution Exposure to Disease

Epidemiology, risk assessment, health tracking, and accountability require information that link environmental exposure to disease. Each of these efforts requires identification of individuals at increased exposures and tools to determine how, and whether, the more exposed individuals show a greater likelihood of increased risk of disease. The inadequacy of exposure assessment in these types of health studies was an underlying premise of the workgroup discussions and findings. In many areas of epidemiological research this may not necessarily be the case, but the workgroup found it a key issue for air pollution epidemiology. The workgroup developed Figure 1 to illustrate the conceptual link between exposure and disease along with the internal pathway from exposure to intake, dose, biological changes, early biological effect, altered structure or function, and finally disease. Historically, scientists have had to rely primarily on measures of exposure and disease

diagnosis to make this link. But the use of better population data, exposure models, exposure biomarkers, and early detection of disease states has improved our ability to explore exposure/disease links (Ryan et al., 2007). We use this conceptual framework both to assess current limitations for health studies applied to air pollution and to identify research opportunities. Based on this framework we characterize information needs and a strategy for our evaluation.

Distinctions among Classical Epidemiology, Risk Assessment, Health Tracking, and Accountability

There are many research, modeling, and evaluation activities that health scientists use to make links between human disease burden and exposures to pollutants. In setting the goals for the work reported here the authors and the workgroup make a distinction among four approaches, two that have been used historically—epidemiology and risk assessment—and two that are emerging—health tracking and accountability. The workgroup found it important to articulate the distinctions among these different approaches both to facilitate the workgroup process and to make sense of the workshop findings. The distinction that the workgroup established among these four approaches to linking disease and exposure are provided in Table 1.

Specific Substances of Interest

Three air contaminants are of interest in the context of this health surveillance and research investigation. These are PM, ozone, and toxic air pollutants. Based on its authority under the Clean Air Act Amendments of 1990, the EPA established a list of 188 toxic compounds. Thus toxic air pollutants are clearly multi-component in nature whereas PM and ozone are generally considered single class of compounds for regulatory purposes. But in the case of PM, recent data on health outcomes suggest that coarse, fine, and ultrafine PM may have different health impacts and could be better characterized as a multi-component pollutant in the future as more information becomes available. In the following paragraphs, we (the authors) discuss the important properties of these substances and their link to human disease.

Particulate Matter

PM measurements are driven largely by efforts to meet target limits for the mass concentration of PM in the urban atmosphere. Important to this process is the selection of a metric by which PM concentration is measured. Some form of mass measurement has been used as the metric for PM

pollution for at least four decades. Over the last two decades, epidemiologic studies have suggested that fine particles are likely more culpable for adverse health effects and regulations have shifted to reflect this. As a result EPA has modified standards to include fine aerosol as a separate class of pollutant.

However, PM is not a single entity. Crustal materials—those dispersed from the soil surface—consisting primarily of carbonates and silicates are likely to have completely different health outcomes when compared to fine or ultrafine particles produced by combustion processes (Spiro and Sligliani, 2003). Diesel exhaust, for example, contains PM with a large fraction of organic material in contrast to the inorganic PM produced in smelting operations. These differing chemical compositions for PM suggest now that determining health outcomes for PM requires alternative strategies that focus on the chemical composition of the PM itself. Sorting PM into different size classes can help address this issue. For example, combustion-related PM sources such as diesel exhaust typically contribute to the fine components of PM, (USEPA, 2004). However, to address specific health outcomes, such as respiratory or cardiovascular diseases, better speciation of PM is necessary.

Ozone

Ozone, a molecule consisting of three oxygen atoms, is a potent oxidant due, in part, to its reactive nature. Ozone reacts with sunlight to produce free atomic oxygen [O(^{3}P)] or reacts with other chemicals in the air to produce odd-oxygen species, which then begin a chain of reactions that lead to photochemical smog. This reactive behavior contributes to the formation of numerous other species ranging from aldehydes and ketones, to peroxyl radicals and excited intermediates (Seinfeld and Pandos, 1998; Finlayson-Pitts and Pitts, 2000; Spiro and Sligliani, 2003). Thus measuring the principal oxidant species, ozone, can give information on other reactive contaminants in the atmosphere. In this way ozone can be a *chemical* surrogate for all oxidizing species to some extent. Ozone is typically monitored in urban settings subject to photochemical smog incidents but usually only during the "ozone season" that typically spans the months of May through September in the US.

Exposure to air containing pure ozone in laboratory settings has demonstrated a relationship between health outcomes and exposure in both animals and in human subjects (Hackney et al., 1976; Hackney et al. 1977; Linn et al., 1978; Linn et al., 1982; Linn et al. 1983; Linn et al., 1988;

Bates, 1995; Lippmann and Schlesinger, 2000). However, in the ambient environment, exposure to other species, most notably the oxidants found in polluted environments, may also be responsible for adverse health outcomes (Ostro, 1993; Catalano et al., 1996; Burnett et al., 1997; Peters et al., 1999; Kinney and Lippmann, 2000; McConnell et al., 2002; Bernstein et al., 2004; Ruidavets et al., 2005). Ozone-measurement systems can be quite specific to the O_3 species, although interferences by water vapor and aromatic hydrocarbons may occur for some analyzers (USEPA, 1997; NARSTO, 1999). Because of the nature of photochemical equilibrium of ozone in the ambient environment, epidemiologic investigations of the health effects of ozone may in effect be using ozone as an *exposure* surrogate for these other species, some of which could be more harmful than ozone itself.

Toxic Air Pollutants

The class of air contaminants referred to as toxic air pollutants or "air toxics" contains numerous chemical compounds with widely varying sources, environmental fate, exposure pathways, and health outcomes. Unlike PM, few health scientists in the last 20 years have suggested that this class of substances can be aggregated into a single entity. Data collection efforts are often broad-based with whole air samples being captured and analyzed for many compounds simultaneously (see for example Hayes, 1989; Eschenbacher et al. 1995; Wallace and Pellizzari, 1995; Delfino, 2002; Kinney et al. 2002; Weisel, 2002; Phillips et al., 2005; and Xue et al., 2005).

The health effects of toxic air pollutants are more difficult to study than those of PM and ozone. While it is relatively easy to examine the effects of compound-specific exposures, in ambient air one encounters different mixtures of toxic air pollutants with transportation sources, industrial sources, and natural sources contributing to varying degrees depending upon location and time of year. The analysis of the impact of air toxics exposure on health remains challenging because of this variability. It may be reasonable to expect non-additive effects on health outcomes associated with simultaneous exposure to a mixture of these compounds. Research is currently focusing on understanding these effects, but results from these short-term exposure studies may not be representative for assessing chronic effects such as cancer, that result from long-term exposures to air toxics. Detecting additive health effects, whether synergistic or antagonistic, currently poses significant challenges.

The Workgroup Process

As leaders of the exposure workgroup, we relied on consensus discussions to identify and evaluate key issues. At the beginning of the workgroup process, the following four questions were presented to the workgroup.

1.   What are the limitations, barriers, and challenges associated with the use of existing environmental, exposure, and health databases or models, and methodologies used to link them, in air pollution health studies including accountability, epidemiologic research, and EPHT?

2.   How can we overcome these limitations, barriers, and challenges?

3.   What are the important emerging health effects and air quality issues for accountability, air pollution health effects research, and EPHT?

4.   In order of priority, what are short- and long-term activities to improve the use and linkage of environmental exposure, health databases, or models for accountability, air pollution health effects research, and EPHT?

The group leaders guided the workgroup effort to apply these questions systematically to PM, ozone, and toxic air pollutants. The group approached this goal by first defining a conceptual framework (Figure 1) within which to address the question of how exposure relates to disease and then used this framework to establish, refine, and address a list of key issues. The group then worked to find overlaps and gaps. A revised list was prepared and again evaluated for overlaps and gaps. The group repeated this process until they achieved consensus. These issues were then used to identify and evaluate methods to overcome these limitations, barriers, and challenges.

The workgroup process identified eight key issues based on consideration of the four questions above. These issues are presented in the next section. During their deliberations to address these four questions, the workgroup discussed the capabilities of new sources of information such as satellite and other remote sensing data and the reliability of modeling exposure from air quality data collected in support of compliance or exposure monitoring. They evaluated technical barriers or communication difficulties in sharing the necessary exposure information between the different research organizations, institutions, or programs. They considered a range of actions from simple, short-term solutions to complex and long-term strategies. The workgroup gave particular attention to the types of data and models needed for source-to-dose characterization at neighborhood, urban, and regional scales. They also considered use of Geographic Information System (GIS)-based inhalation exposure models for application to PM, ozone, and toxic air pollutants and the impact of

location, mobility, activity (breathing rates and micro-environment), and demographics on estimated inhalation rates for PM, ozone, and toxic air pollutants. The workgroup considered specific actions such as the use of census data to locate populations relative to air pollution concentrations with adjustments to account for population mobility. Finally, they considered the feasibility and value of constructing population exposure distributions by combining (1) spatially and temporally resolved estimates of ambient concentrations of specific air pollutants; (2) geo-coded time-location-activity survey data; (3) specific exposure microenvironments; and (4) breathing rates, which vary by age, gender, and activity level.

Information Needs

In the framework outline shown in Figure 1, hazard and exposure information relevant to health tracking includes source/emissions data, environmental monitoring data, biological monitoring data, time-activity-location data for the exposed population, and other available and relevant data (e.g., from questionnaires and diaries, including past and current exposures and exposure factors). In spite of the clear need for health tracking to make use of environmental factors to classify populations with respect to hazards, there is limited capacity for such activities within communities, state agencies, and federal agencies. The need to build this capacity across a broad range of agencies and communities was a key factor in defining the workshop evaluation strategy.

Emerging Issues

Dose reconstruction is becoming important in a number of health studies. The ability to back-calculate the magnitude and source of exposure adds value to epidemiology studies as well as health tracking and accountability studies. But reliable dose reconstruction requires a combination of information on sources, exposures, and markers of dose (see, for example, McKone et al., 2007). It is important to recognize that even when there is an abundance of information on exposure biomarkers, there may not be sufficient information to establish source-to-dose links. For example (Sohn et al., 2004) have illustrated some of the problems in dose reconstruction even in cases where there is good temporal data on tissue concentrations. As noted by Ryan et al. (2007) there is a continuum of information that must be assembled in order to use exposure biomarker data to establish source-to-dose links. Improving this process is an emerging area of research in health effects research.

Recent studies reveal that the spatial and population resolutions required for exposure tracking depend on whether one is tracking ambient-source pollutants, such as those found in ambient air, or tracking surface water or indoor/product-based pollutants, such as those found food, soil, consumer products, indoor releases, etc. (Lobscheid and McKone, 2004; Marshall et al., 2005; McKone et al., 2007). There is heterogeneity of ambient pollutant intake due to the geographic distribution of sources, variation among pollutants in dispersion patterns from the same source, population mobility, and indoor/outdoor exposure levels. In addition, many contaminants of interest in environmental health research can be associated with both regional concentrations and local- or even indoor-source peak levels. For example, people are exposed to PAHs as a result of living in a region with a large number of sources, but they are also exposed as a result of their proximity roadways and to neighborhood-scale wood burning (Lobscheid and McKone, 2004). Food residues and indoor releases from cooking may provide additional important exposure pathways to some of these substances.

In addition to the difficulty of linking exposure with proximity to pollutant emissions, there are complex links between exposure and health effect. For many pollutants, there are significant differences between exposure and intake, intake and dose, and dose and effect. Using ambient pollutants as an example, one notes that variations in breathing rates, diet, activity health status, and genetic susceptibility can cause individuals with the same exposure to respond differently. Thus, differences in activity levels, metabolic rates, health status, and other factors can contribute to significant differences in health impacts for individuals experiencing very similar pollutant exposures. This means that in order to improve the links between exposure and disease at a population scale, one will need to collect, store, and evaluate this type of information at a level that provides detailed sub-population and even individual data on these factors.

Results

In this section, we identify the eight key issues identified by the workshop and provide the workshop findings about each of these key issues in the context of limitations, barriers, and challenges. We then provide and set priorities for actions to understand limitations, remove barriers, and confront challenges.

Findings on the Key Issues

  (1) Differential Exposures

    Exposures to a number of air pollutants are differential in the sense that exposure is not proportional to the relative outdoor concentrations of these pollutants. Time-activity allocations and mobility (e.g., commuting) and micro-environmental and building infiltration factors are among the main factors that modify human exposures to outdoor pollutants. Very reactive gaseous contaminants such as ozone often display indoor-outdoor ratios that are very low due to their reactions with surfaces in indoor environments as well as indoor, gas-phase reactions. Typical indoor-outdoor ratios for ozone range from 0.1-0.4 with the low end of these values found in air-conditioned buildings in summer and the high end observed when windows are open and residences are well ventilated (Romieu et al., 1998; Lee et al., 1999; Geyh et al., 2000; Lee et al., 2004). Gaseous pollutants of intermediate reactivity, including nitrogen dioxide, display indoor outdoor ratios of about 0.5 in the absence of sources indoors (Rojas-Bracho et al., 2002; Ryan et al., 1988; Spengler et al., 1994). While there are few sources of ozone indoors, nitrogen dioxide is produced indoors by combustion so the presence of combustion appliances strongly affects this ratio. Non-reactive gas-phase contaminants display indoor-outdoor ratios approaching unity. Based on several studies done in locations around the world, typical ratios measured for benzene, for example, center on 0.9 (Son et al., 2003; Adgate et al., 2004; Serrano-Trespalacios et al., 2004). Again, the presence of sources, e.g., an attached garage, can markedly affect this ratio. Particulate matter can be partially filtered by the building envelope resulting in indoor-outdoor ratios less than unity. Various studies have found indoor-outdoor ratios for $PM_{2.5}$ to center on 0.6 (Geller et al., 2002; Bennett and Koutrakis, 2006). Such ratios can, again, be markedly affected by indoor sources including cooking activities, use of tobacco products, cleaning activities (Singer et al., 2006), and general activity associated with house occupants. Because of this, researchers often use tracers unique to outdoor air, e.g., sulfate, to measure effective penetration of particulate matter.

    While the summary numbers presented here may indicate that the exposure experienced by individuals could still be approximated using a constant multiple of outdoor concentrations, the variability of time spent indoors and outdoors as well as the variability in these penetration ratios precludes such a simple analysis. Personal activities, including amounts of time spent in each microenvironment, as well as differential use of products that produce indoor sources suggest that the relationship between ambient air concentrations of these contaminants and personal exposures is

not simple. Personal exposures experienced by individuals in a population can be lower, approximately equal, or higher than those inferred from ambient pollutant concentrations. Thus, to assess such exposures, exposure researchers need detailed measurement of personal exposures or more detailed exposure models that are based on knowledge of individual activities as well as variations in indoor and ambient concentrations. Population exposures may average out these differences, but exposures experienced by individuals, including those in "small" epidemiologic investigations are likely to be strongly influenced by variations among individuals' non-ambient contributions to overall exposure.

(2) The Impact of Location and Mobility

Mobility and time spent in locations away from a primary residence greatly influence people's exposures to a number of pollutant emissions—both indoors and outdoors. This is particularly important when one has geographically based exposure information rather than personal exposure monitoring data. The majority of exposure information for PM, ozone, and toxic air pollutants comes from stationary monitoring data, pollutant transport models and/or some combination of monitoring data and model results. However, regardless of the approach used to obtain concentration data, when population exposures are linked to a specific location (census track, zip code, street address) without adjustments for mobility and location changes, estimated individual exposures can differ significantly from actual exposures. For example, near- and on-roadway exposure to motor-vehicle pollutants will be greater than the exposures to same pollutants while subjects are indoors at home, at work or at school. Location and mobility can be captured by the use of personal monitoring—but this remains expensive, intrusive and time-consuming. Therefore, the near-term likelihood is low for obtaining the large quantities of personal exposure data needed for health impact studies. The remaining alternative is the use of stochastic exposure models that make use of hierarchical Bayesian or other "ground-truthing" methods to calibrate exposure modeling with appropriate exposure indicators. For example Marshall et al. (2005) made use of regional air pollution model combined with driving diaries in the South Coast (Los Angeles area) air basin to adjust exposure estimates to account for mobility and time spent in locations away from home relative to exposures assigned based on residence location.

(3) Biologically Relevant Time Scales

Biologically relevant time-scales of exposure to pollutants vary among the different classes of pollutants (e.g., minutes for some VOCs to hours or days or years for PM). Thus, measurement and

exposure characterization for these different air pollutants have to be consistent with appropriate biological and dose-response periods.

Time scales for exposure and health effects have often been characterized as acute, sub-chronic, and chronic (See for example USEPA, 2001). Acute exposures are those that occur over short time scales lasting from a few seconds to a few hours. Examples include exposures under accidental release scenarios, photochemical smog incidents, or incidents such as the London Fog episode. Such episodes are characterized by short-duration and high-pollution concentrations that usually dissipate to background levels after a relatively short period. Effects may be catastrophic, such as might occur with an acute carbon monoxide exposure episode or the occurrence of a fatal asthma attack. Less catastrophic effects may result in visits to the hospital emergency department, simple irritation, or no clinically observable effect. Because short-duration, high-impact pollutant concentrations are very difficult to predict, measurement of such exposures is problematic.

Sub-chronic effects occur over times scales ranging from a few days to about 30 days duration. Synoptic and some seasonal pollution effects may occur over this type of time scale (Barry and Chorley, 1998). Health outcomes of interest in such situations are less well defined than for acute changes in exposure.

Chronic exposures occur over longer durations up to and including lifetime exposure. The health impacts of interest here are chronic diseases and those, such as cancer, with a long induction period. In such cases, it is of interest to measure exposures integrated over long periods. Such a need suggests alternative measurement strategies differing in intent and, perhaps, instrumentation, from those used in acute investigations.

In developing measurement strategies, the biological outcome of interest must be considered. For example, if acute effects are to be understood properly, then fine time-resolution data must be collected. One solution, albeit an expensive and burdensome one, is to monitor for the contaminant of interest on a real-time basis. This is a costly undertaking for some pollutants in that most of the measurements can be at background levels with only a small number of such measurements truly of concern. On the other end of the time scale, chronic exposures and concomitant health outcomes do not need such detailed time resolution while short-term studies of a few days, or even a few weeks duration do not supply the information needed to assess the risk or impact of a lifetime of exposures. For example, measurement of toxic air-pollution exposures for a week during the summer months gives little insight into the lifetime exposure likely experienced by any individual.

Further, measurement in a single location, given the mobility of the population (Chapin, 1974; Klepeis et al., 2001), may be insufficient to determine health impacts associated with the "true" exposures.

The development of a measurement strategy for health research studies must account for biologically relevant time scales for data collection. If short-term effects are the target, then real-time data collection may be the only solution. For chronic effects, excursions of short duration, even if quite spectacular, are unlikely to influence long-term exposure. Selecting an optimum measurement or modeling-based exposure prediction strategy has to be based on consideration of the time scale over which the biological effect occurs.

(4) Age-Specific Exposure Issues

Exposure issues are not the same for all ages. As an example, for children and older adults, exposures are quite different than those of younger adults. These issues are important for understanding exposure vulnerability, as well as biological sensitivity or susceptibility of population groups to air pollutants.

Monitoring strategies must take into account the target population. Children, adolescents, adults, and the elderly have vastly different exposure profiles due to different activities they undertake as well as vastly different susceptibility to identical exposures. While younger children spend the majority of their time in their own homes, older children may spend much more time outdoors. Adults spend a significant fraction of their time in work environments, some with significant occupational exposures (Klepeis et al., 2001). Children, especially the very young, may have incompletely developed immune and neurological systems. For example, exposures to lead in the very young may result in irreversible cognitive impairment while similar exposure to an adult would not give rise to such adverse consequences (Needleman, 1993; Muldoon et al. 1996; Lanphear et al., 2005). Similarly, in the elderly, exposure to contaminant concentrations similar to those of younger adults may lead to very different outcomes. An elderly person, with reduced lung capacity or a compromised cardiovascular system may exhibit catastrophic effects from exposure to PM or carbon monoxide at levels that would result in no observable difficulties for a robust young adult. There is a large literature on this topic. As examples see: Gong et al., 2005; Fung et al., 2006; Martins et al., 2006; Sarnat et al., 2006; or Vallejo et al., 2006. The workgroup also considered that an immune-compromised adult may suffer substantially greater adverse effects from exposure to the

same level of contaminant than his or her healthy counterpart, but did not identify a study to confirm this.

Health scientists developing plans for an exposure evaluation must recognize the age-specific exposure differences within a population and account for these differences in health studies. This is necessary to protect both the vulnerable members of society as well as those who are robust. A properly designed monitoring program takes this into account. Air pollution standards are often derived to protect sensitive subgroups within the population. These are often children, the elderly, and those with chronic conditions that compromise their ability to mitigate exposure effects. As discussed more fully in the accompanying Symposium paper by Thurston et al. (2007), a number diseases of emerging importance such as, multiple sclerosis, autism spectrum disorders, and other immunological disorders pose significant challenges to health researchers due to long latency between exposure and diagnosis.

(5) Exposures to Multiple Pollutants

In an epidemiologic analysis of air pollution health effects, the contributions from PM and other co-pollutants (e.g. ozone, NO_2 and combustion-related air toxics) can be interwined. Moreover, differences in PM size and chemical composition are important factors for cross-sectional analysis of PM and co-pollutant health effects. Both the spatial and temporal differences in sources and concentrations of air pollutants of health concern can be quite complex across large metropolitan or urban areas. Within cities, the spatial variability of concentrations of PM and its species near roadways tend to be large. In particular, near-roadway concentrations of ultra fine PM, combustion-related gases, and air toxics are often influenced by mobile source emissions. Human contact with these localized peaks in concentrations tends to occur more during commuting or walking near busy roads. However, homes, schools, or workplaces located near these roads may also experience greater levels of ambient pollutant infiltration indoors. Consequently, source-specific contributions of PM and other pollutants may vary significantly by location (e.g., ambient outdoors, indoors, commuting, etc.), by season and type of microenvironment. Diurnal or temporal variability in the contributions from different sources of PM and air toxics not only influence the composition of air pollution mixture in various microenvironments but also their relative toxicity to humans. Human exposures to these pollutants depend strongly on the behavioral patterns of individuals. Therefore, the covariance between these behavioral factors and concentrations of PM, ozone and air toxics can be quite complex and variable among individuals. Hence, relating stationary outdoor air pollution

monitoring data to realistic exposures of individuals or to population exposures to multiple pollutants requires the use of sophisticated measurement and modeling information. Monitoring of multiple pollutants in key outdoor and indoor microenvironments, along with personal exposure measurements, are often needed to generate the necessary information. Typically, these data are then used in conjunction with either land-use regression modeling (Jerret et al., 2005; Ross et al., 2005) or air quality dispersion modeling (Isakov et al., 2006) in estimating concentrations of pollutants of interest at different outdoor human receptor locations. Personal exposure estimates may then be produced by using either empirical or mechanistic human exposure models. The mechanistic exposure models, such as the SHEDS model (Burke et al., 2001), incorporate information on sources and concentrations of pollutants in different microenvironments with corresponding human contact data derived from available time-activity diaries. The application of these more refined exposure estimation methodologies in multi-pollutant health effects studies has been considered more recently (English et al., 1999; Isakov and Özkaynak, 2007).

6) Tracking Effect Modifiers

An effect modifier in the context of an epidemiologic health study refers to a variable that influences the magnitude of the association between an exposure measure and the health outcome studied. Some exposure-related factors may also influence either the composition or the toxicity of the selected or indicator pollutant. Some examples of potential effect modifiers that show up in health effects studies for PM and toxic-air pollutants are: 1) prior or concurrent exposures to air pollutants that are not recorded, 2) spatial and temporal variation in concentrations and /or composition of PM and toxic air pollutants by region, 3) temporal changes in the residential indoor-outdoor air exchanges influencing infiltration of outdoor pollutants indoors, 4) differences among households in air conditioning and window usage, 5) differences among households in combustion appliance type and use, presence of attached garages, consumer product use, exposure to second-hand smoke, and 6) age, occupation and susceptibility-based exposure differences among the study subjects.

These factors may play an important role in the outcome of the research, tracking, and accountability investigations considered here. In particular, when any of these evaluations are based on either geographic or temporal contrasts between different population groups, the variations in the effect modifiers could influence either the results or interpretation of study findings. Consequently,

there is a need to understand the impacts of these and other likely effect modifiers in order to assess their contribution to the health endpoints appropriately across populations, study areas, and time.

(7) Tracking Exposures for Long-Latency Outcomes

Some diseases are separated by long latency periods between the environmental exposures that potentially give rise to or promote a disease and the frank presentation of the disease. These diseases provide a particular challenge to epidemiology, health tracking, accountability, and risk assessment. Among the diseases with very long latency periods (on the order of decades) are cancer, amyotrophic lateral sclerosis (ALS), and a large number of age-related diseases (heart disease, osteoarthritis, diabetes, skin disorders, eye disorders, etc.). To explore any potential links between onset of these diseases and environmental exposures in early life requires long-term exposure tracking. Many other diseases can have latency periods on the order of years that add to the complexity of constructing any postulated exposure-disease link (Thurston et al., 2007). This is particularly important in cases where disease incidence might be enhanced by both recent and long-term (years or more cumulative exposures). Examples of diseases in this category include early childhood diseases, development of asthma, autoimmune diseases, autism spectrum disorders and neurological disorders such as, multiple sclerosis and attention deficit-hyperactivity disorder.

There are a number of options for confronting the complexity of tracking exposures for long-latency outcomes. One approach is to be resourceful in methods used to reconstruct historical exposures. An example is the enormous efforts that have been expended for the Hiroshima/Nagasaki populations with regard to radiation exposure reconstruction (Marchetti and Straume, 1996). Another approach is to make use of long-lived biomarkers of exposure. Here again the radiation community has set the pace (Lucas, 1997), but there have been efforts of this sort for chemicals (Chen and McKone, 2001). Another option is to make use of early markers of effect that link both to recent exposures and to occurrence of disease later in life in or in off-spring (Ryan et al., 2007). One example of this is the use of chromosomal aberrations that are key precursors to later disease (Chen and McKone, 2001).

(8) Short Scale Exposure-Outcome Tracking

The etiology of many chronic diseases (such as cardiovascular disease, asthma, and cancer) is complex and involves the a mix of genetic and environmental factors interacting with each other

over hours, days, months, or years. Recent studies have demonstrated clear links between short-term increases in exposure to PM and increases in incidence of cardiovascular events (Zanobetti and Schwartz, 2005; Pope et al., 2006), changes in cardiopulmonary markers of inflammation (Rückerl et al., 2006; Pope et al., 2004), and in asthma (Gilmour et al., 2006). Efforts to track short-term peaks in exposure to pollutants such as PM, ozone, and toxic air pollutants are constrained both by the technical feasibility of deploying monitoring networks with sufficient scale and coverage to capture the appropriate level of population, spatial, and temporal variation and the lack of financial resources to support and maintain such a network. Clearly there is a need to build capacity to deploy, maintain, and track a network of sensors that can track short-term (hours to days) exposure profiles for PM, ozone, and toxic air pollutants.

Confronting Limitations, Barriers and Challenges

Limitations, Barriers and Challenges—PM

The workshop process also identified several issues that impose limitations, barriers, and challenges to efforts to improve studies of the health impacts of PM. Key among these is better understanding of PM speciation and how this relates to health impacts for all types of health impact studies—epidemiology, risk assessment, health tracking and accountability. Similarly, better resolution of spatial and temporal variations of PM concentrations is important to all types of health studies. This includes variations that derive from land use (such as urban/rural differential and near or far from roadway classifications), seasonal variations, and transient events. For example, the emerging evidence for links between cardiac disease and short-term PM exposure places high value on future studies that match transient events to specific populations such as populations served by a particular hospital (Kunzli et al., 2005). This appears to also be relevant to the exacerbation of asthma and the ability to collect hospital data on an exposed population, or in some cases, to use school questionnaires (Mortimer et al., 2004, Roberts et al., 2006).

Limitations, Barriers and Challenges—Ozone

The workshop process identified several issues that impose limitations, barriers, and challenges to efforts to improve studies of the health impacts of ozone. A key problem is the paucity of methods and opportunities to link medical surveillance to individual measures of exposure. There is a lack of personal exposure information for ozone. Ambient ozone measurements have not been

linked well to specific microenvironments resulting in a significant barrier to improving the resolution of exposure-disease links. Because current ozone monitoring programs are motivated by compliance with the ambient standard, and they usually operate from May through September, there are very few ozone data available for characterizing annual exposures. This is a barrier to studies that need data on combined exposures to ozone and PM during winter months. But this barrier is easily overcome by simply monitoring ozone together with PM throughout the year at existing sites. Other challenges for ozone are improving geographic coverage of exposure data and making upstream links to the ultimate sources that account for observed ozone concentrations. There is also the challenge of making more effective use of models and monitoring data to map out ozone exposures in space and time. Finally, there is the challenge of getting more information about indoor microenvironments—including, residences, schools, and vehicles. Ozone concentrations are generally much lower indoors. To address these limitations, one requires more ozone measurements in these particular microenvironments, together with activity-based exposure models that can be calibrated against these data. Without this information large uncertainties will remain along with the potential for significant exposure misclassification.

Limitations, Barriers and Challenges—Toxic Air Pollutants

The workshop process also identified several issues that impose limitations, barriers, and challenges to efforts to improve studies of the health impacts of toxic air pollutants. Differential exposure and how this relates to health impacts is important for all types of health impact studies— epidemiology, risk assessment, health tracking and accountability. As was the case for PM, better resolution of spatial and temporal variations of toxic-air pollutant concentrations are important to all types of health studies. This includes variations that derive from geographical location (such as urban, rural, proximity to roadways or point sources), seasonal variations, and transient events. Because toxic air pollution includes a mixture of different substances, it is important to have better information on how the composition of this mixture may vary among different generic geographic locations (urban, suburban, rural) as well as among different specific locations (Boston, Detroit, Los Angeles, Oakland, etc.). A further challenge in the case of toxic air pollutants is that many of these pollutants reach humans through multiple pathways—making geographic and even site-specific air monitoring data less useful for exposure classification. For example, many toxic air pollutants are emitted to the indoor environment by cooking, smoking or wood fires (Zhang and Smith, 2003) and some of the larger and more persistent polycyclic aromatic hydrocarbons (PAHs) enter humans

primarily through ingestion and the dietary pathway (Lobscheid et al. 2004). In these cases there is not only the potential for exposure misclassification but also problem of inconsistencies in exposure estimated or inferred from biomonitoring (for example hydroxy-PAH levels in urine) and exposure inferred from ambient measurements. In addition, the uptake and toxicodynamics of air toxics such as PAHs may differ significantly based on whether the PAHs are ingested, inhaled, or absorbed dermally.

Defining and Setting Priorities for Action

The workshop participants identified limitations, barriers and challenges but also identified efforts to overcome these issues, and then set priorities among these efforts. In this section we summarize priorities for short-term and long-term goals to improve PM, ozone, and toxic air pollutant exposure data for accountability, air pollution health effects research, EPHT, and public health surveillance studies.

We consider the recommendations below the first step in a long-term process for improving the contributions of exposure information to health studies. It is important to note that even though the workshop process did set priorities, the participants found themselves constrained by lack of information about the scope of the misclassification problem. Therefore, participants identified the following as their first priority:

> *Evaluate the nature and magnitude of exposure misclassification problem for different types of health effects studies*. This requires some exploratory case studies that illustrate how limitations in exposure information can improve the statistical power to test hypothesized associations in health surveillance research.

> *Continue to convene the types of symposia and workgroup efforts*. The efforts here are a starting point but cannot end with one symposium.

> *The health science community must become more aware of and active in practicing homologous matching—that is matching the space and time scales of pollutants, diseases and populations*. Each pollutant has a characteristic reach and effective lifetime. Human populations also have characteristic geographic regions in which they migrate and temporal activity scales. Diseases also play out with complex time histories. The link between sources of pollutants and any disease outcome requires better sense of how the overlap of spatial and temporal patterns among pollutants, populations, and diseases plays out to make exposure-disease connections.

PM – Priority Activities

For PM and for the range of health research studies considered here, the long- and short-term strategies include the effective use of models and monitoring. In contrast to ozone and toxic air pollutants the existing monitoring network for PM has more spatial and temporal resolution. Moreover, there have been many studies of indoor/outdoor relationships for PM exposure. But information on speciation is limited. In the short term, models can be used to make more relevant but less reliable (relative to monitoring data) empirical estimates of the variation of PM speciation among different generic (urban/rural) and specific geographic regions. For example, Lobsheid et al., (2007) have demonstrated that monitoring data for PM2.5, which has more spatial and temporal resolution than does PAH measurement data, can be calibrated to make proxy estimates of PAH composition of the particles.

Accountability and risk assessment can profit from improved modeling along with efforts to capture better both variability and uncertainty in the PM exposure estimates. Air pollution epidemiology and risk assessment will benefit from early effort to select a limited set of locations for detailed speciation. This effort can identify whether and how much exposure difference there is among different generic locations, e.g., coastal/inland, near road/away from road. In addition, this effort could also inform both addition exposure research and improved monitoring strategies. Finally, this effort should strive to characterize different geographical scales—from community to urban, regional and even continental background.

Health tracking studies can benefit from efforts to improve the scope of PM monitoring and exposure tracking. One area that that can be addressed in the short-term is the need to track exposures during short-term, high-exposure events. For example, rapidly deployable monitors in mobile systems can be used to track PM concentrations during forest fires and agricultural burning. There is also the potential for stratified deployment of monitors for unique events—such as heat waves or weather conditions that trap high PM levels.

In the long term the broad range of health research efforts will profit significantly from (i) increasing the number of continuous monitoring sites, (ii) conducting routine ultra-fine monitoring at key sites, and (iii) the co-location PM and PM speciation monitoring.

Ozone – Priority Activities

The workshop participants ranked priority activities based in terms of context of the various health research areas—air pollution epidemiology, risk assessment, health tracking, and accountability. In the case of ozone and for the full range of health research studies, a short-term priority is the need to integrate models and limited measurements to provide more information on indoor-environment exposures, and a short but also longer-term priority is more personal exposure measurements. There is also a need for capturing baseline ambient data throughout the year and in a broader range of environments—not just summertime measurements in urban hot spots.

For air-pollution epidemiology, risk assessment and accountability exposure uncertainty is an important limitation and a barrier to improved classification. The first priority is to characterize and communicate this uncertainty for specific geographic areas. This effort will help researchers understand and confront the reliability of exposure information and the level of confidence placed in these data for health research. Better communicating uncertainty about ozone should also give insight on the best short and long-term strategies for improving the reliability of exposure information.

For health-tracking the highest priority is expanded monitoring to characterize better ozone exposures for specific communities and sub-populations. This is particularly important for communities whose health status is being monitored as part of an existing community health study. But health tracking can also profit in the short-term from systematic integration of modeling and limited monitoring data. For example, the EPA-CDC PHASE project has demonstrated how hierarchical Bayesian methods (Fuentes and Raftery, 2005; McMillan et al., 2008) can improve the temporal and spatial resolution of air pollution exposure information (Boothe et al., 2005; Haley et al., 2007). But so far this approach has been retrospective. Accountability and risk assessment are health studies that require these types of efforts for making projections of future exposures.

Toxic Air Pollutants – Priority Activities

The need among all health research studies for better spatial and temporal resolution of toxic air pollutant exposures can be addressed in the short-term with modeling improvements but in the long-term will require more personal, community, and food monitoring. As in the case of PM, in the short term, improved modeling efforts can provide preliminary, but less reliable improvements in spatial/temporal resolution relative to a long-term effort at personal monitoring. For example, the

hierarchical Bayesian method used in the EPA-CDC PHASE project has demonstrated improvement in the spatial and temporal resolution of modeling in a first set of case studies. However, the US-wide spatial/temporal resolution provided by the PHASE approach may be limited in certain geographical areas and for some pollutants, for the purposes of tracking and epidemiology studies. This issue may be addressed either by increasing the spatial resolution in the PHASE process or by employing hybrid modeling approaches, which combine local and regional scale modeling results (e.g., Isakov and Özkaynak 2007) relevant to each application. The approach used in the EPA-CDC PHASE project or similar approaches could also be extended to toxic air pollutants if routine measurement of toxic air pollutants were to be made. Also in the short term, models can be used to assess differential exposures attributable to both indoor and dietary sources of toxic air pollutants. In the long-term, there is a need for a systematic effort to monitor and model population variability in cumulative intake of toxic air pollutants from ambient air, indoor air, water, and food. An important resource for this effort is the NHANES biomonitoring data. Although NHANES data do not capture regional variability, it does provide information on the magnitude and variation of exposures to many pollutants including toxic air pollutants. Interpretation of the biomonitoring data can, however, be problematic, especially for those air toxics that have short lifetimes in the body.

An emerging opportunity for increasing the utility of the NHANES data is the development of state-level biomonitoring programs. California has now established a state-level biomonitoring effort and we expect that other states will follow. The ability to contrast biomonitoring data from a national-scale and state or local-scale population provides an important opportunity to detect and understand competing exposure pathways (see for example McKone et al., 2007).

Overarching Issues

One of the over-arching lessons of this symposium is that obtaining better exposure information for disease surveillance, risk assessment, accountability and tracking requires both setting goals for what is needed and mapping out the pathway from current capabilities to these goals. Meeting these long-term goals requires definition of incremental steps that provide useful information for the interim and move the endeavor toward the long-term goals. Meeting these goals may also require increased resources and research infrastructure—issues that must be addressed by environmental and health agencies, policy makers, and legislatures at both the state and federal level.

The need for better health indicators at the community health often motivated the types of health research that were considered in this symposium. We recognize that communications between the community members and health researchers is an important aspect of both exposure and health surveillance research. Detailed discussion of these issues and how they relate to exposure information was not the key goal of this symposium, which was more focused on technical improvements. But the symposium participants recognized and noted that, while technical methods and scientific findings inform the health research process, they often fail to provide information that is relevant or meaningful to stakeholders. Work to date has focused on the technical aspects of obtaining and linking data, and less emphasis has been placed on the significance of representing and interpreting such data for non-technical audiences. This issue relates both to transparency and the need to share information effectively and a timely manner with other agencies and organizations.

Another over-arching theme among the three different pollutants and the different health study approaches is the need for integration among alternate exposure assessment approaches. For example, different groups may advocate exposure indicators, biomonitoring, mapping methods (e.g., GIS), modeling, environmental media monitoring, and/or personal exposure modeling. However, the workgroup discussions and observations of emerging research reveal that the greatest progress comes from integrations among two or more of these efforts (see for example McKone et al., 2007; Nuckols et al., 2004; Sohn et al. 2004).

In the results above, we distinguish the findings among three pollutants—PM, ozone, and toxic air pollutants—and four health research areas—air pollution epidemiology, risk assessment, health tracking, and accountability. This approach is useful for finding important differences. For example consider the expanding role of models. They are most useful for accountability but helpful also for epidemiology and tracking. Models can be used to detect small changes in exposure and health benefits that an epidemiology study could not find. Researchers must be careful to recognize that, although models can be set up to provide detailed results in space and time, model and parameter uncertainties may limit the reliability of such detailed results.

There are overlapping research needs and opportunities among these different health research strategies—epidemiology, health tracking, and accountability. When these health research strategies are applied to PM, ozone, toxic air pollutants, accurate classification of individual exposures must include adjustments based on a geographical measure of proximity to hazard. Personal measures of

exposure will fail to correlate with local source contributions from multiple sources and locations, including indoor sources, unless adjustments are made for contributions from indoor and near-home sources, such as near-roadway sources. There is a need to improve methods for combining the geographic distributions of environmental factors with information on human population distributions and human activities in order to identify and evaluate those factors that provide reliable indicators of the magnitude and source of population exposures. Finally, reflecting back on Figure 1, we note the need to consider the continuum of indicators from emissions to exposures to dose to disease in order to identify better the critical exposure related information that is most relevant to advancing our knowledge on air pollution health impacts.

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Table 1   Distinctions among epidemiology, risk assessment, health tracking and accountability

| Epidemiology |
| --- |
| *Environmental epidemiology is "the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems" (Last, 2001). It has a strong focus on finding populations without and with a given disease (or with clearly higher disease incidence) to identify factors in the population with disease, such as harmful substance exposures that explain the relative risk of disease in the exposed population. The focus of "classical" epidemiology is on the distribution of diseases and their determinants within populations in contrast to a focus on markers of disease or on clinical populations.* |
| **Risk assessment** |
| *An environmental health risk assessment uses information about sources and emissions of toxic substances to estimate the probability of harm for people who might be exposed to these substances. The approach is prospective, essential going from source to dose to disease risk. Either epidemiology data or toxicology studies with animals are used to construct dose-response relationships. Risk assessments, prepared by EPA and other agencies, are used to determine if releases and environmental levels of toxic substances pose an unacceptable risk as defined by regulatory standards and requirements. A risk assessment does not measure the actual health effects and often does not measure actual exposures but may use emissions data and models to infer exposures. Conservative safety margins are typically built into a risk assessment analysis to ensure protection of the public.* |
| **Health tracking** |
| *Environmental public health tracking (EPHT) is the ongoing systematic collection, integration, analysis, interpretation, and dissemination of data about environmental hazards, exposure to environmental hazards, and health effects potentially related to exposure to environmental hazards. EPHT focuses on the integration of medical surveillance data with environmental indicators (proximity to emissions sources, air quality indicators, etc) and with exposure tracking measurements (pollutant concentrations in air, water, food etc). In contrast to epidemiology, which tends to be retrospective and more strongly focused on accurate disease classification rather that exposure tracking, and in contrast to risk assessment, which is prospective and more focused on providing sufficient margins of safety, EPHT focuses on linking both disease to emissions and emissions to disease. It is much more broadly focused on integrating information among multiple substances and indicators, works in both prospective and retrospective modes, and emphasizes a broader range of disease endpoints and exposure indicators. In contrast to direct measurement of exposure, exposure indicators are surrogate measures that imply potential or actual exposures, for example proximity to roadways or blood levels of pollutants.* |
| **Accountability** |
| *Accountability has a focus on linking actions to outcome. The goal is to use some combination of epidemiologic data, risk assessment modeling, and health tracking data to "account" for how much health benefit will accrue from an action, such as reducing emissions for a specific facility or for a class of emissions (i.e. off-road diesel, railroads, coal-fired power plants). Accountability has much more emphasis on going from disease or some metric of potential disease (disease biomarkers) back to actions to control the sources that are responsible for that endpoint. For example, heart disease incidence in a population can be attributable to many factors (diet, life style, genetics, and air pollution). An accountability study would strive to make an accurate assessment of how reductions in air pollution could affect heart disease in the context of these other factors.* |
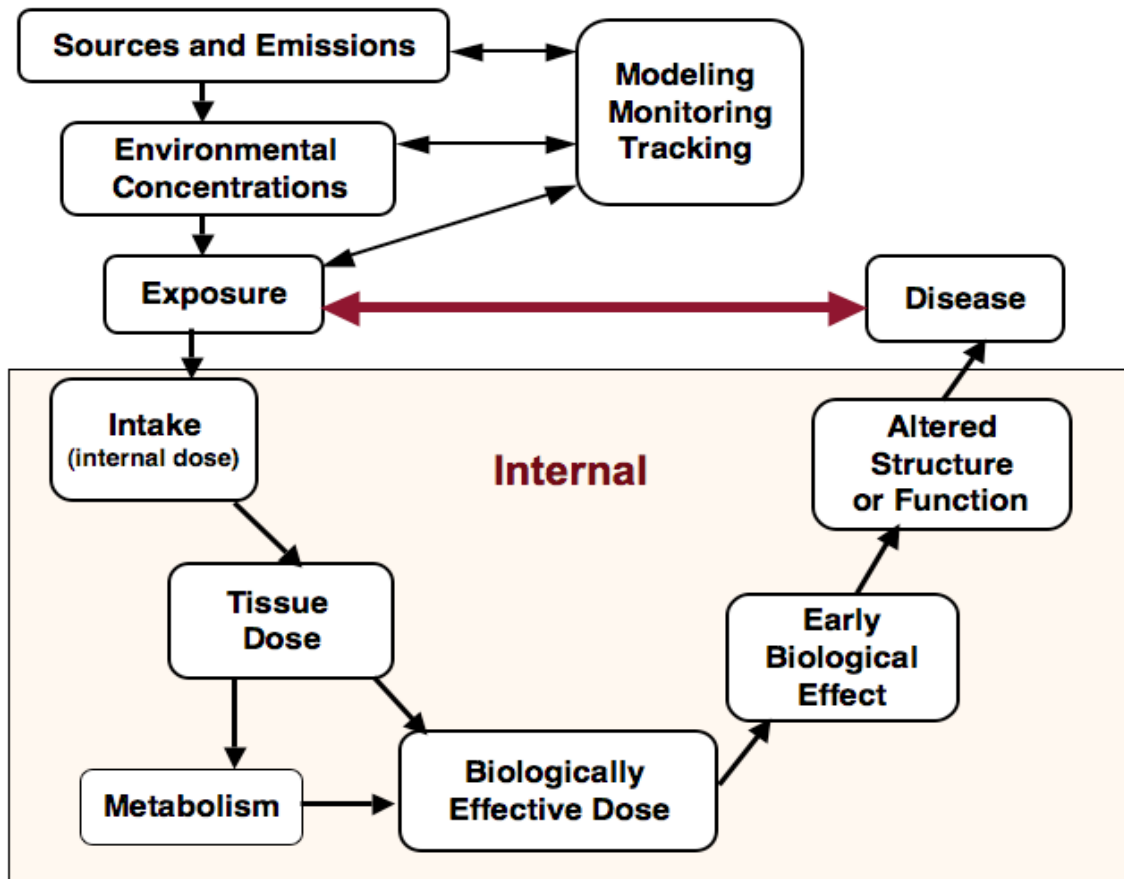
Figure 1. Conceptual framework indicating the links among exposure information, modeling, monitoring, tracking, and disease.