HEI

SPECIAL REPORT 16

November 2007

Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects

A Special Report of the Institute's Air Toxics Review Panel

EXECUTIVE SUMMARY

ABOUT HEI

The Health Effects Institute is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the effects of air pollution on health. To accomplish its mission, the Institute

- Identifies the highest-priority areas for health effects research;
- Funds and oversees the conduct of research projects;
- Provides intensive independent review of HEI-supported studies and related research;
- Integrates HEI's research results with those of other institutions into broader evaluations; and
- Communicates the results of HEI research and analyses to public and private decision makers.

Typically, HEI receives half of its core funds from the U.S. Environmental Protection Agency and half from the worldwide motor vehicle industry. Additional funds for this Special Report were provided by the U.S. Federal Highway Administration.

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INTRODUCTION

Air toxics are emitted into ambient air from many different sources. They comprise a diverse group of air pollutants that, with sufficient exposure, are known or suspected to cause adverse effects on human health, including cancer, effects on the development of organs or tissues, and damage to the immune, neurologic, reproductive, or respiratory systems. Tools and techniques for assessing project-specific health effects of mobile-source air toxics (MSATs) are very limited. Indeed, there are substantial uncertainties about the health effects of ambient levels of air toxics in general, irrespective of their source allocation. While acknowledging these uncertainties, the U.S. Environmental Protection Agency (EPA), in its model-based National Air Toxics Assessment (NATA), estimated that 92% of the U.S. population is at some increased risk for adverse effects on the respiratory system (including irritation and other effects) because of exposure to air toxics from outdoor sources. The NATA also estimated that, in most of the U.S., people have a slightly increased lifetime risk of cancer from air toxics (between 1 and 25 in a million) if they are exposed to 1999 concentrations of these pollutants over the course of their lifetimes. Comparisons of total air toxics emissions by state indicated that heavily industrialized urban areas have the highest emissions.

MSATs are a subset of these air toxics. They are compounds emitted by on-road vehicles and non-road equipment that are known or suspected to cause cancer or other serious health effects and environmental effects (*http://epa.gov/otaq/toxics.htm*). In its 2001 rule, the EPA listed 21 compounds or compound classes as MSATs. In the more recent 2007 rule, the EPA expanded this list. Mobile sources are the principal sources of exposure for only a few of these MSATs because many are also emitted by non-mobile sources. The EPA estimates that mobile sources are responsible for about 44% of estimated outdoor emissions of air toxics. Almost 50% of the estimated cancer risk and 74% of the estimated noncancer risk from air toxics is estimated to come from mobile sources.

This Executive Summary is excerpted from HEI Special Report 16, *Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects*, by the Institute's Air Toxics Review Panel. The entire report is available at *www.healtheffects.org* or from HEI.

This report is based on work supported by the Federal Highway Administration (under Cooperative Agreement No. DTFH61-04-H-00048) and by other HEI sponsors. Any opinions, findings, and conclusions or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the Federal Highway Administration or other HEI sponsors.

Hazardous air pollutants, of which air toxics can be considered a subset, were defined in the authorizing legislation for the 1970 Clean Air Act as "pollutants which present, or may present, through inhalation or other routes of exposure, a threat of adverse human health effects (including, but not limited to, substances which are known to be, or may reasonably be anticipated to be, carcinogenic, mutagenic, teratogenic, neurotoxic, which cause reproductive dysfunction, or which are acutely or chronically toxic)." A U.S. air toxics regulatory program was authorized under the Act and redesigned under the 1990 Clean Air Act amendments. The legislation required the EPA to characterize, prioritize, and address the effects of air toxics on public health and the environment. It also required the EPA to regulate or consider regulating air toxics from motor vehicles in the form of standards for fuels, vehicle emissions, or both. The 1990 amendment to the Act specifically included acetaldehyde, benzene, 1,3-butadiene, and formaldehyde—all known or suspected carcinogens.

The EPA also addressed urban air toxics in its Integrated Urban Air Toxics Strategy. The strategy addressed toxic emissions from all outdoor sources, including stationary, area, and mobile sources. It promised a rulemaking on mobile-source standards in 2000 and new area-source standards to take effect by 2009. The Integrated Urban Air Toxics Strategy included a list of 33 high-priority hazardous air pollutants, including acetaldehyde, acrolein, benzene, 1,3-butadiene, formaldehyde, and polycyclic organic matter (POM).

By considering pollutants that originate at least in part from mobile sources and taking into account health and risk-assessment information in the Integrated Risk Information System (IRIS), the EPA in 2001 defined a list of 21 MSATs, which was expanded in 2007. This approach, including the regulation of fuels and vehicle emissions as well as the introduction of emission-control devices such as catalytic converters, has led to substantial reductions in the emission of MSATs since the enactment of the Clear Air Act. It contrasts with the approach taken for the criteria air pollutants (CO, SO_x, NO_2, O_3, lead, and particulate matter [PM]), for which national ambient air quality standards for compounds were established.

Taking into account expected future reductions in air toxics from existing regulatory programs designed to reduce ozone and PM (including the reformulated-gasoline program, the national low emission vehicle program, emissions standards for passenger vehicles, gasoline sulfur-control requirements [Tier 2], and heavy-duty diesel-fuel sulfur-control requirements), the EPA has elected only recently to issue additional fuel and vehicle standards to further control MSATs.

In 2007, the EPA issued a new rule to reduce hazardous air pollutants from mobile sources. This rule identifies 1162 MSATs, but singles out 8 MSATs as key: benzene, 1,3-butadiene, formaldehyde, acetaldehyde, acrolein, POM, naphthalene, and diesel exhaust (DE). The 2007 rule also limits the benzene content of gasoline and reduces emissions from passenger vehicles and gas cans. Reformulated or alternative fuels have been introduced since 1992 with expectations of substantial environmental benefits, as their emission profiles are different from those of traditional fuels. These changes are resulting in decreases in the emissions of some MSATs and increases in others. However, the introduction of reformulated or alternative fuels might pose its own risks, and the removal of individual fuel components does not automatically ensure safe fuels.

In addition to the broad public-health issues they pose, a concern over the health risks of MSATs influences the development of transportation projects at the federal, state, and local levels. Under the National Environmental Policy Act of 1969 as amended in 1982, agencies such as the U.S. Federal Highway Administration are expected to address MSAT effects associated with transportation projects that are intended to create new capacity or add significantly to urban highways or highways close to potentially vulnerable populations. Local projects that lead to improvements in traffic flow, expansion of bus routes, and vehicle-technology retrofits all influence the quantities and sites of MSAT emissions. In some cases, the possible environmental and public-health effects of MSATs have been part of the basis for legal challenges to such projects. In this climate of increased regulatory, public, and judicial concern about MSATs, an MSAT review panel was formed by the Health Effects Institute (HEI) in the winter of 2005. The panel was charged with the following tasks:

- Use information from the peer-reviewed literature to summarize the health effects of exposure to the 21 MSATs defined by the EPA in 2001;
- Critically analyze the literature for a subset of priority MSATs selected by the panel; and
- Identify and summarize key gaps in existing research and unresolved questions about the priority MSATs.

In creating this review of the literature on MSATs, the panel focused on a subset of MSATs for which mobile sources are a sizable source of human exposure and for which existing data suggested that health effects might be observed at concentrations approaching those found in ambient air. The panel elected not to focus on a critical review of DE, a substantial contributor to human exposure and to health risks in the overall context of MSATs, because HEI and many others (e.g., the EPA and the California Air Resources Board) have recently reviewed these issues. Instead, the panel has provided an expanded summary of DE reviews. The seven priority MSATs selected for detailed review by the panel were acetaldehyde, acrolein, benzene, 1,3-butadiene, formaldehyde, naphthalene, and POM. For each of these, the panel asked three questions—(1) To what extent are mobile sources a significant source of exposure to this MSAT? (2) Does this MSAT affect human health? and (3) Does this MSAT affect human health at environmental concentrations? The panel then reviewed the peer-reviewed literature, reached key conclusions, and made recommendations for future research.

SUMMARY

Ambient MSATs usually occur as part of complex mixtures. They are emitted into ambient air from many different sources and can also be present in water, food, and soil. MSATs can exist in the gas phase as well as in association with PM. Moreover, after emission, some MSATs can undergo atmospheric transformations that produce other known MSATs, products of unknown chemistry and toxicity, and nontoxic degradation products. In this report, the panel focused on the sources of MSATs—motor vehicles, particularly on-road motor vehicles—for which the broadest evidence exists. Non-road sources, such as trains, planes, and marine vessels, which are important but less studied, were not considered. Substantial exposures to many MSATs also come from sources other than motor vehicles.

Source attribution suggested that the contribution of mobile sources to overall emissions is greatest for 1,3-butadiene, followed by benzene, formaldehyde, acetaldehyde, and acrolein. Mobile-source contributions to overall POM exposure vary depending on the POM species; however, it is clear that mobile sources are contributors to POM associated with PM. There are insufficient data on mobile-source contributions to naphthalene exposure, but it appears likely that the contributions of mobile sources to exposures are limited. Given that substantial exposures to certain MSATs can arise from non-mobile sources (e.g., smoking, food, and indoor environments) and can occur through air, water, food, and soil, regulatory authorities beyond those specified in the Clean Air Act would be required to substantially reduce overall human exposure to these toxic agents.

Because exposures to MSATs occur as complex mixtures (which can also include non-MSAT compounds), it is especially difficult to deconvolute the contributions of any given compound to human health risks. Animal toxicology studies, typically concerning exposure to single compounds, provide insights into targets and underlying mechanisms of toxicity and dose–response. But these insights are constrained by uncertainties about extrapolations from high to low doses and about interspecies comparisons. Because relatively high levels of exposure are found in occupational settings, studies of occupational cohorts provide opportunities for understanding associations between exposure to individual MSATs and health effects. Epidemiologic studies in occupational cohorts have served, accordingly, to define risks associated with exposures to several MSATs. Identifying effects in community studies is more challenging, however, because of low ambient concentrations, exposures to multiple possible toxicants, and other confounders. Nonetheless, newer studies incorporating biomarkers that directly reflect individual exposure and early biologic

consequences can reduce confounding due to misclassification errors in exposure and provide important insights into possible health effects of certain MSATs. They may be especially useful in occupational studies with low exposure concentrations and, to a more limited extent, in community settings.

ACETALDEHYDE

1. To what extent are mobile sources an important source of exposure to acetaldehyde?

Mobile sources are a significant, but not the principal, source of exposure to acetaldehyde. Concentrations tend to be lowest outdoors; they are 2 to 10 times higher indoors and in vehicles. Acetaldehyde is also present in many foods.

2. Does acetaldehyde affect human health?

Like all aldehydes, acetaldehyde is chemically reactive. It causes irritation to the eyes, skin, and respiratory tract and induces cellular inflammation. Although acetaldehyde is a carcinogen in rodents, the data on the possibility of its carcinogenicity in humans are inadequate. Data on respiratory effects are limited mainly to small clinical studies of asthmatic patients using exposure challenges with aerosols of acetaldehyde. The effects of exposures to multiple aldehydes, all of which can be irritants to the respiratory tract, are not known.

3. Does acetaldehyde affect human health at environmental concentrations?

There has been only one epidemiologic study of environmental exposure to acetaldehyde. This was a study of children with asthma, and it was small and unable to distinguish the effect of acetaldehyde from that of other pollutants. Inasmuch as indoor sources of acetaldehyde account for most personal exposure and ambient concentrations appear to be far below those producing irritation, it is doubtful that acetaldehyde in ambient air at concentrations observed in recent years has adversely affected human health. It is likely, however, that acetaldehyde emissions will increase with current requirements for increased use of ethanol, although the exact effect on future concentrations is not known.

ACROLEIN

1. To what extent are mobile sources an important source of exposure to acrolein?

Because of the limited number of studies of acrolein, its highly reactive nature, and the limitations of sampling methods, the available environmental data for acrolein might not be sufficient to allow an assessment of ambient, indoor, or personal exposures. Additional limitations include the number and type of environments sampled, the number of samples collected, the absence of accounting for the presence or absence of sources, the absence of data on geographic and seasonal variability, the representativeness of residences and populations sampled, and the lack of sampling for sensitive or at-risk populations. Limited urban roadside and in-vehicle data do not suggest elevated exposures. Surprisingly low concentrations were observed in tunnel studies—a finding at odds with EPA estimates that overall contributions of acrolein from mobile sources are considerably higher. Substantial mobile-source contributions to exposure might result from the formation of acrolein from 1,3-butadiene in the air. Environmental tobacco smoke is a major indoor source of acrolein.

2. Does acrolein affect human health?

Acrolein is very irritating to the respiratory tract of humans and animals. Studies showed that chronic inhalation resulted in inflammation. Although acrolein might damage DNA, several animal bioassays have not provided substantive evidence of carcinogenicity. Because of its high chemical reactivity, acrolein is unlikely to be distributed throughout the body.

3. Does acrolein affect human health at environmental concentrations?

There are insufficient data for an assessment of the effect of ambient exposures to acrolein on human health. However, it should be noted that measured environmental concentrations and personal exposures were only slightly lower than concentrations shown to cause irritation.

BENZENE

1. To what extent are mobile sources an important source of exposure to benzene?

There are more air-monitoring data for benzene than for any other MSAT considered in this report. The highest concentrations were found at urban roadside and urban in-vehicle locations. Mobile sources are an important component of overall exposure to benzene. Consistent with this observation, levels of personal exposures to benzene appeared to be in the same range as those found in ambient settings.

2. Does benzene affect human health?

There is clear and widely accepted evidence from a variety of occupational epidemiologic studies that exposure to benzene increased the risks of acute myeloid leukemia; there is less certainty about other lymphohematopoietic cancers. Extended follow-up of an existing cohort further confirmed this association. Moreover, data from several new cohorts (petroleum workers and gas and electric utility workers) demonstrated increased leukemia risks at lower estimated exposures than previously observed.

3. Does benzene affect human health at environmental concentrations?

Some studies have indicated that an increased risk of childhood leukemia was associated with proximity to petrochemical works and gasoline stations, although identifying such effects in community studies is challenging. Studies have yielded mixed results with regard to associations between traffic and childhood leukemia. There has been substantial progress in the development of biomarkers for benzene. Studies using biomarkers have indicated a relationship between benzene concentrations in

urine and the presence of cytogenetic abnormalities in community studies (e.g., in street vendors, gasoline-service-station attendants, and children attending schools near major roads). Variations in the enzymes involved in the metabolism of benzene have been identified and linked to increased sensitivity to benzene hematotoxicity. Several newer studies have revealed effects on hematologic indices at lower exposure concentrations than those reported before. However, there remains considerable uncertainty as to the lowest concentration that might be associated with adverse hematologic effects.

1,3-BUTADIENE

1. To what extent are mobile sources an important source of exposure to 1,3-butadiene?

Mobile sources are the most important contributors to 1,3-butadiene concentrations in ambient air in most locales. Because of 1,3-butadiene's short atmospheric lifetime, concentrations of 1,3-butadiene are highest near sources. However, its high reactivity results in the production of other MSATs, such as formaldehyde, acetaldehyde, and acrolein. Several recent studies indicated that indoor concentrations might be higher than outdoor concentrations—an effect not entirely accounted for by environmental tobacco smoke (a known source of indoor exposure). Thus, there might be other important sources of indoor exposure.

2. Does 1,3-butadiene affect human health?

The human evidence, though limited, is consistent with the possibility that 1,3-butadiene causes lymphohemato-poietic cancers in high-exposure occupational settings. This is plausible, moreover, because there is good evidence that certain metabolites of 1,3-butadiene cause cancer and adverse reproductive effects in mice. In humans, however, the metabolism of 1,3-butadiene appears to be more like that of rats, a less susceptible species. At high exposure concentrations, such as those once found in the U.S. in certain industries, 1,3-butadiene is likely to be a human health hazard because of its carcinogenicity. The confounding of 1,3-butadiene's health effects by coexposure to styrene and dimethyldithiocarbamate cannot be ruled out. But on epidemiologic and toxicologic grounds, 1,3-butadiene seems likely to be the active agent. Biomarkers of exposure for 1,3-butadiene have been developed and validated. However, biomarkers of effect were identified inconsistently in exposed workers and were not correlated with biomarkers of exposure.

3. Does 1,3-butadiene affect human health at environmental concentrations?

In community studies, there is no direct evidence of health effects of exposure to 1,3-butadiene at ambient concentrations. However, community studies have limitations in sensitivity because of the low exposure concentrations and other pollutants present.

FORMALDEHYDE

1. To what extent are mobile sources an important source of exposure to formaldehyde?

Indoor sources of formaldehyde appear to be the principal source of exposures. Indoor concentrations are three to five times higher than outdoor concentrations. However, mobile sources are an important source of ambient concentrations. The highest ambient concentrations were found at urban roadside sites. It appears that summer photochemical activity contributes more formaldehyde to ambient air than do direct vehicle emissions, as strong seasonal effects are observed. It is important to note that in Brazil, ambient formaldehyde concentrations have increased fourfold over the past few years, following the expansion of the fleet of vehicles using compressed natural gas.

2. Does formaldehyde affect human health?

Like the other aldehydes, formaldehyde is an irritant to the eyes, skin, and respiratory tract in humans. It has recently been classified as a human carcinogen, in part because of evidence of nasopharyngeal cancer at concentrations historically encountered in industrial settings. The underlying mechanisms of this carcinogenicity are not fully understood but include DNA–protein crosslinking and increased cell proliferation.

3. Does formaldehyde affect human health at environmental concentrations?

There is limited and inconclusive evidence that indoor exposure to formaldehyde increases the occurrence of asthma in children. There is no evidence about health effects of outdoor exposures to ambient concentrations of formaldehyde, but given the likelihood of the expanded use of alternative fuels in the U.S. and the probable resulting increases in formaldehyde emissions, some attention should be paid to possible effects of increased emissions from mobile sources in the future.

NAPHTHALENE

1. To what extent are mobile sources an important source of exposure to naphthalene?

Naphthalene is the most abundant polycyclic aromatic hydrocarbon (PAH) found in ambient air. Mobile sources (both fuel combustion and evaporation) are an important, but not the primary, source of naphthalene. There is limited evidence to suggest that concentrations of naphthalene are higher at roadside sites and in vehicles. Indoor concentrations are typically 5 to 10 times higher than ambient concentrations and may be derived from environmental tobacco smoke and moth repellents. However, trends toward the reduction of these indoor sources might lead to the increased importance of outdoor sources as determinants of exposure.

2. Does naphthalene affect human health?

There is evidence in rodents that exposure to naphthalene leads to inflammation of the nasal tract and tumors of the nasal epithelium and olfactory epithelium. However, there are no data

on carcinogenicity in humans. Several case reports, which were deficient in quantitative exposure assessments, suggest that single or repeated exposures can cause effects in blood cells, such as hemolysis and hemolytic anemia.

3. Does naphthalene affect human health at environmental concentrations?

There are no epidemiologic or other studies that assess the health effects of exposure to naphthalene at ambient concentrations.

POM

1. To what extent are mobile sources an important source of exposure to POM?

POM is a term commonly used to describe a mixture of hundreds of chemicals, including PAHs, their oxygenated products, and their nitrogen analogs. Some POMs are found in the gas phase, some in the particle phase, and some in both. Different measurement studies have looked at different POM mixtures; there is no standard exposure- or health-based definition of POM. There is a lack of consistency in PAH groupings and indicator compounds for POM. Mobile sources might be significant contributors to ambient concentrations of POM in urban settings. However, other combustion processes, such as wood burning, cigarette smoking, road paving, and roof tarring might lead to substantial additional exposures. Food-derived sources of POM are likely to be the principal source of exposure in many settings where there is limited combustion of wood and industrial fossil fuel. Diesel vehicles emit more PAHs than gasoline-fueled vehicles; "cold starts" account for up to 50% of their PAH emissions.

2. Does POM affect human health?

A few PAH components of POM are potent animal carcinogens. Some of these (e.g., benzo[a]pyrene) are classified as human carcinogens. At high occupational exposures, there is sufficient evidence for increased risk of lung cancer in coke-oven workers and possibly in asphalt-industry workers. An association between lung cancer and the use of "smoky" coal in China has also been observed. In highly polluted industrial sites, adverse effects on reproductive (lower birth weights), respiratory (obstructive lung disease), cardiovascular (ischemic heart disease), and immune (enhanced allergic inflammation) systems have been reported, but the linkages to POM are not firm.

3. Does POM affect human health at environmental concentrations?

While there is evidence that air pollution containing PAHs is genotoxic and has effects on reproductive health, there is no direct evidence from community studies that POM specifically, at ambient exposure concentrations, causes health effects. Because community studies involve exposures to complex mixtures, they have limited ability to address the effects of POM alone. Additional identification of relevant biomarkers of exposure is needed.

GAPS AND RECOMMENDATIONS

Several common themes emerged when the panel considered the gaps in current research on exposure to MSATs and their health effects. It is evident that exposure to many MSATs comes from sources other than vehicles. Indeed, mobile sources are the primary sources of exposure for only a few of the 21 MSATs listed by the EPA in its 2001 mobile-source rule. There is a clear need for better attribution of the sources of these MSATs by, for example, measuring concentrations at roadsides and in vehicles. There is also a need for better attribution of the other sources of MSATs, as well as better characterization of concentrations in microenvironments, such as homes and workplaces, and of factors that affect these concentrations. In addition, there is a need for better characterization of the contributions of outdoor concentrations to indoor concentrations and personal exposures. The atmospheric transformation products of some MSATs and the factors regulating their production need to be identified and characterized. Efforts should also be made to collect existing MSAT data from local and state monitoring networks and enter these data into useable, readily accessible databases to support further analyses.

Improved analytical chemistry methodologies are needed to better understand exposure measures. For example, measured concentrations of acrolein appear to be lower than the actual ambient concentrations. This discrepancy might reflect technical limitations of conventional measurement techniques. There is a strong need to compile spatial and trend data on MSATs in the U.S. Very limited information on these topics is available in the peer-reviewed literature. There is also a need to continue improving the NATA modeling estimates of exposures to MSATs. While in many instances the NATA estimates were similar to exposure concentrations reported in the literature, there were some instances, particularly among aldehydes, in which the NATA modeling appeared to substantially underestimate measured exposure concentrations. Improved modeling and better characterization of spatial and temporal trends are vital to the assessment of the effect of regulatory changes on the emissions of MSATs. They are also needed to assess possible changes in MSAT emissions arising from increased utilization of alternative fuels. Indeed, the widespread introduction of ethanol and compressed natural gas as vehicle fuels in some regions of the world that have less advanced engine and emission control technologies than the U.S. has already led to increases in ambient concentrations of aldehydes in these regions. Whether or not the same increases will be seen in the U.S. as alternative-fuel use increases is unknown.

The risk of cancer has dominated health concerns about the MSATs. The panel concluded the following:

- Quantitative estimates of the relationship between cancer risk and exposure concentrations have been derived largely from studies of occupational cohorts in which exposure to high concentrations of one or more MSATs

could be documented. Data from these occupational cohorts might be of limited utility in the evaluation of health effects at ambient concentrations because of the magnitude of the exposure differences. At this point, the panel does not recommend initiating new cohort studies in areas where exposures come from ambient settings to improve quantitative estimates of the cancer-causing potential of MSATs. Moreover, the cost, methodologic difficulties, and data challenges make it unlikely that there are feasible epidemiologic approaches capable of addressing the risks associated with ambient exposures on a compound-by-compound basis. Substantial improvements in the analytical sensitivity and specificity of biomarkers for key MSATs might provide firmer linkages between exposures and health effects; however, it will be important to validate these biomarkers first. Epidemiologic studies coupled with the use of such biomarkers will be of value in investigating the health effects of mobile-source emissions as a whole—for example, looking at populations living or working in proximity to roadways. Research opportunities for use of biomarkers might also arise in connection with emerging "hot spots."

- Some quantitative cancer-potency estimates for MSATs have been derived from animal models. However, extrapolating from these results to humans remains troublesome. A better understanding of the toxicokinetics (including biotransformation pathways) of MSATs in both animals and humans, particularly at ambient concentrations, might provide clearer perspectives on the similarities and dissimilarities between animal and human metabolism. However, the issue of potential species differences in toxicodynamics will remain.
- Animal studies and especially epidemiologic studies have tended not to focus on noncancer endpoints in investigating the toxicity of MSATs. It remains an open question as to whether developmental, reproductive, and neurologic effects result from mobile-source exposures and to what extent the MSAT aldehydes, singly and collectively, contribute to pulmonary irritation, cough, and asthma. Subpopulations susceptible to the health effects of MSATs also need to be better defined.

Air Toxics Review Panel

HEI Air Toxics Review Panel. 2007. Mobile-Source Air Toxics: A Critical Review of the Literature on Exposure and Health Effects. HEI Special Report 16. © 2007 by the Health Effects Institute, Boston, Mass. The entire report is available at *www.healtheffects.org* or from HEI.

Health Effects Institute, Charlestown Navy Yard
120 Second Avenue, Boston, MA 02129-4533
Phone: +1-617-886-9330. Fax: +1-617-886-9335. *www.healtheffects.org.*