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APPENDIX I

HEALTH EFFECTS

SEPTEMBER 2012

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INTRODUCTION

This document presents a summary of scientific findings on the health effects of ambient air pollutants. The California Health and Safety Code Section 40471(b) requires that the South Coast Air Quality Management District prepare a report on the health impacts of particulate matter in the South Coast Air Basin (SCAB) in conjunction with the preparation of the Air Quality Management Plan revisions. This document, which was prepared to satisfy that requirement, also includes the effects of the other major pollutants.

HEALTH EFFECTS OF AIR POLLUTION

Ambient air pollution is a major public health concern. Excess deaths and increases in illnesses associated with high air pollution levels have been documented in several episodes as early as 1930 in Meuse Valley, Belgium; 1948 in Donora, Pennsylvania; and 1952 in London. Although levels of pollutants that occurred during these acute episodes are now unlikely in the United States, ambient air pollution continues to be linked to increases in illness (morbidity) and increases in death rates (mortality).

The adverse health effects associated with air pollution are diverse and include:

- Increased mortality
- Increased health care utilization (hospitalization, physician and emergency room visits)
- Increased respiratory illness (symptoms, infections, and asthma exacerbation)
- Decreased lung function (breathing capacity)
- Lung inflammation
- Potential immunological changes
- Increased airway reactivity to a known chemical exposure - a method used in laboratories to evaluate the tendency of airways to have an increased possibility of developing an asthmatic response
- A decreased tolerance for exercise.

The evidence linking these effects to air pollutants is derived from population-based observational and field studies (epidemiological) as well as controlled laboratory studies involving human subjects and animals. There have been an increasing number of studies focusing on the mechanisms (that is, on learning how specific organs, cell types, and biochemicals are involved in the human body's response to air pollution) and specific pollutants responsible for individual effects. Yet the underlying biological pathways for these effects are not always clearly understood.

Although individuals inhale pollutants as a mixture under ambient conditions, the regulatory framework and the control measures developed are mostly pollutant-specific. This is appropriate, in that different pollutants usually differ in their sources, their times and places of occurrence, the kinds of health effects they may cause, and their overall levels of health risk. Different pollutants, from the same or different sources, may sometimes act together to harm health more than they would acting separately. Nevertheless, as a practical matter, health scientists, as well as regulatory officials, usually must deal with one pollutant at a time in determining health effects and in adopting air quality standards. To meet the air quality standards, comprehensive plans are developed such as the Air Quality Management Plan (AQMP), and to minimize toxic exposure a local air toxics control plan is also prepared. These plans examine multiple pollutants, cumulative impacts, and transport issues related to attaining healthful air quality. A brief overview of the effects observed and attributed to various air pollutants is presented in this document.

This summary is drawn substantially from reviews presented previously (SCAQMD, 1996, 2003, 2007), and from reviews on the effects of air pollution by the American Thoracic Society (ATS, 1996), the U.S. EPA reviews for ozone (U.S. EPA, 2006), Carbon Monoxide (U.S. EPA, 2010), and Particulate Matter (U.S. EPA, 2004, 2009), from a published review of the health effects of air pollution (Brunekreef and Holgate, 2002), and from reviews prepared by the California EPA Office of the Environmental Health Hazard Assessment for Particulate Matter (Cal EPA, 2002) and for Ozone (Cal EPA, 2005). Additional materials are from EPA's current review of the ozone standard and health effects (EPA, 2011). More detailed citations and discussions on air pollution health effects can be found in these references.[1]

[1] Most of the studies referred to in this appendix are cited in the above sources. Only more recent specific references will be cited in this summary.

OZONE

Ozone is a highly reactive compound, and is a strong oxidizing agent. When ozone comes into contact with the respiratory tract, it can react with tissues and cause damage in the airways. Since it is a gas, it can penetrate into the gas exchange region of the deep lung.

The EPA primary standard for ozone, adopted in 2008, is 0.075 ppm averaged over eight hours. The California Air Resources Board (CARB) has established standards of 0.09 ppm averaged over one hour and at 0.070 ppm averaged over eight hours.

The major subgroups of the population considered to be at increased risk from ozone exposure are outdoor exercising individuals, including children, and people with preexisting respiratory disease(s) such as asthma. The data base identifying the former group as being at increased risk to ozone exposure is much stronger and more quantitative than that for the latter group, probably because of a larger number of studies conducted with healthy individuals. The adverse effects reported with short-term ozone exposure are greater with increased activity because activity increases the breathing rate and the volume of air reaching the lungs, resulting in an increased amount of ozone reaching the lungs. Children may be a particularly vulnerable population to air pollution effects because they spend more time outdoors, are generally more active, and have a higher ventilation rate than adults.

A number of adverse health effects associated with ambient ozone levels have been identified from laboratory and epidemiological studies (EPA, 1996; 2006, 2011; ATS, 1996). These include increased respiratory symptoms, damage to cells of the respiratory tract, decrease in lung function, increased susceptibility to respiratory infection, and increased risk of hospitalization.

Increases in ozone levels are associated with elevated absences from school. The Children's Health Study, conducted by researchers at the University of Southern California, followed a cohort of children that live in 12 communities in Southern California with differing levels of air pollution for several years. A publication from this study reported that school absences in fourth graders for respiratory illnesses were associated with ambient ozone levels. An increase of 20 ppb ozone was associated with an 83% increase in illness-related absence rates (Gilliland, 2001).

The number of hospital admissions and emergency room visits for all respiratory causes (infections, respiratory failure, chronic bronchitis, etc.) including asthma

shows a consistent increase as ambient ozone levels increase in a community. These excess hospital admissions and emergency room visits are observed when hourly ozone concentrations are as low as 0.06 to 0.10 ppm.

Numerous recent studies have found positive associations between increases in ozone levels and excess risk of mortality. These associations persist even when other variables including season and levels of particulate matter are accounted for. This indicates that ozone mortality effects may be independent of other pollutants (Bell, 2004).

Multicity studies of short-term ozone exposures (days) and mortality have also examined regional differences. Evidence was provided that there were generally higher ozone-mortality risk estimates in northeastern U.S. cities, with the southwest and urban mid-west cities showing lower or no associations (Smith, 2009; Bell, 2008). Another long-term study of a national cohort found that long-term exposures to ozone were associated with respiratory-related causes of mortality, but not cardiovascular-related causes, when PM2.5 exposure were also included in the analysis.

Several population-based studies suggest that asthmatics are more adversely affected by ambient ozone levels, as evidenced by increased hospitalizations and emergency room visits. Laboratory studies have attempted to compare the degree of lung function change seen in age and gender-matched healthy individuals versus asthmatics and those with chronic obstructive pulmonary disease. While the degree of change evidenced did not differ significantly, that finding may not accurately reflect the true impact of exposure on these respiration-compromised individuals. Since the respiration-compromised group may have lower lung function to begin with, the same degree of change may represent a substantially greater adverse effect overall.

Another publication from the Children's Health Study focused on children and outdoor exercise. In communities with high ozone concentrations, the relative risk of developing asthma in children playing three or more sports was found to be over three times higher than in children playing no sports (McConnell, 2002). These findings indicate that new cases of asthma in children are associated with heavy exercise in communities with high levels of ozone. While it has long been known that air pollution can exacerbate symptoms in individuals with respiratory disease, this is among the first studies that indicate ozone exposure may be causally linked to asthma onset.

In addition, human and animal studies involving both short-term (few hours) and long-term (months to years) exposures indicate a wide range of effects induced or associated with ambient ozone exposure. These are summarized in Table I-1.

TABLE I-1

Adverse Health Effects of Ozone (O3) - Summary of Key Studies

0_3 CONCENTRATION AND EXPOSURE HR., PPM	**HEALTH EFFECT**
Ambient air containing 0.10 - 0.15 daily 1-h max over days to weeks; ≥ 0.05 (8 hour average)	Decreased breathing capacity, in children, adolescents, and adults exposed to 0_3 outdoors Exacerbation of respiratory symptoms (e.g., cough, chest pain) in individuals with preexisting disease (e.g., asthma) with low ambient exposure, decreased temperature, and other environmental factors resulting in increased summertime hospital admissions and emergency department visits for respiratory causes
≥0.12 (1-3h) ≥0.06 (6.6h) (chamber exposures)	Decrements in lung function (reduced ability to take a deep breath), increased respiratory symptoms (cough, shortness of breath, pain upon deep inspiration), increased airway responsiveness and increased airway inflammation in exercising adults Effects are similar in individuals with preexisting disease except for a greater increase in airway responsiveness for asthmatic and allergic subjects Older subjects (>50 yrs old) have smaller and less reproducible changes in lung function Attenuation of response with repeated exposure
≥0.12 with prolonged, repeated exposure (chamber exposures)	Changes in lung structure, function, elasticity, and biochemistry in laboratory animals that are indicative of airway irritation and inflammation with possible development of chronic lung disease Increased susceptibility to bacterial respiratory infections in laboratory animals

From: SCAQMD, 1996; EPA, 2007

Some lung function responses (volume and airway resistance changes) observed after a single exposure to ozone exhibit attenuation or a reduction in magnitude with repeated exposures. Although it has been argued that the observed shift in response is evidence of a probable adaptation phenomenon, it appears that while functional changes may exhibit adaptation, biochemical and cellular changes which may be

associated with episodic and chronic exposure effects may not exhibit similar adaptation. That is, internal damage to the respiratory system may continue with repeated ozone exposures, even if externally observable effects (chest symptoms and reduced lung function) disappear.

In a laboratory, exposure of human subjects to low levels of ozone causes reversible decrease in lung function as assessed by various measures such as respiratory volumes, airway resistance and reactivity, irritative cough and chest discomfort. Lung function changes have been observed with ozone exposure as low as 0.06 to 0.12 ppm for 6-8 hours under moderate exercising conditions. Similar lung volume changes have also been observed in adults and children under ambient exposure conditions (0.10 - 0.15 ppm). The responses reported are indicative of decreased breathing capacity and are reversible.

The results of several studies where human volunteers were exposed to ozone for 6.6 hours at levels between 0.04 and 0.12 ppm were recently summarized (Brown, 2008). As shown in the figure below, there is an increasing response on lung function with increasing exposure levels in moderately exercising subjects.

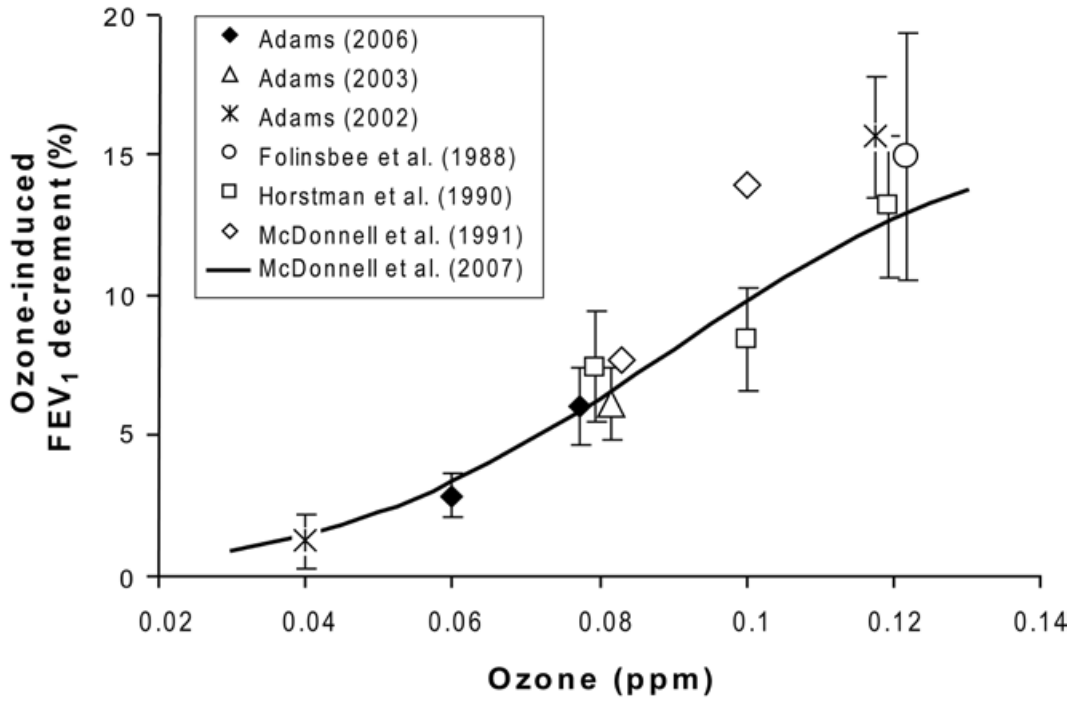

FIGURE I-1

Comparison of mean ozone-induced decrements in lung function following 6.6 hours of ozone exposure (from Brown, 2008)

In addition to controlled laboratory conditions, studies of individuals exercising outdoors, including children attending summer camp, have shown associations of reduced lung function with ozone exposure. There were wide ranges in responses among individuals.

Results of epidemiology studies support the relationship between ozone exposure and respiratory effects. Several, but not all, studies have found associations of short-term ozone levels and hospital admissions and emergency department admissions for respiratory-related conditions (EPA, 2011).

In laboratory studies, cellular and biochemical changes associated with respiratory tract inflammation have also been consistently reported in the airway lining after low level exposure to ozone. These changes include an increase in specific cell types and in the concentration of biochemical mediators of inflammation and injury such as cytokines and fibronectin. Indications of lung injury and inflammatory changes have been observed in healthy adults exposed to ozone in the range of 0.06 to 0.10 ppm.

The susceptibility to ozone observed under ambient conditions could be due to the combination of pollutants that coexist in the atmosphere or ozone may actually sensitize these subgroups to the effects of other pollutants.

Some animal studies show results that indicate possible chronic effects including functional and structural changes of the lung. These changes indicate that repeated inflammation associated with ozone exposure over a lifetime may result in sufficient damage to respiratory tissue such that individuals later in life may experience a reduced quality of life in terms of respiratory function and activity level achievable. An autopsy study involving Los Angeles County residents provided supportive evidence of lung tissue damage (structural changes) attributable to air pollution.

A study of birth outcomes in southern California found an increased risk for birth defects in the aortic and pulmonary arteries associated with ozone exposure in the second month of pregnancy (Ritz et al., 2002). This is the first study linking ambient air pollutants to birth defects in humans. Studies conducted since mostly focusing on cardiac and oral cleft defects have found mixed results, with some showing associations, but others did not. Confirmation by further studies is needed.

In summary, adverse effects associated with ozone exposures have been well documented, although the specific causal mechanism is still somewhat unclear.

It may be instructive to provide the overall EPA staff preliminary conclusions on the causality on ozone health effects for the health outcomes evaluated (EPA, 2011). These are provided in the two tables below.

TABLE I-2

Summary of Causal Determinations for Short-Term Exposures to Ozone

HEALTH CATEGORY	CAUSAL DETERMINATION
Respiratory Effects	Causal relationship
Cardiovascular Effects	Suggestive of a causal relationship
Central Nervous System Effects	Suggestive of a causal relationship
Effects on Liver and Xenobiotic Metabolism	Inadequate to infer a causal relationship
Effects on Cutaneous and Ocular Tissues	Inadequate to infer a causal relationship
Mortality	Likely to be a causal relationship

From EPA, 2011

TABLE I-3

Summary of Causal Determinations for Long-Term Exposures to Ozone

HEALTH CATEGORY	CAUSAL DETERMINATION
Respiratory Effects	Likely to be a causal relationship
Cardiovascular Effects	Suggestive of a causal relationship
Reproductive and Developmental Effects	Suggestive of a causal relationship
Central Nervous System Effects	Suggestive of a causal relationship
Carcinogenicity and Genotoxicity	Inadequate to infer a causal relationship
Mortality	Suggestive of a causal relationship

From EPA, 2011

PARTICULATE MATTER

Airborne particulates are a complex group of pollutants that vary in source, size and composition, depending on location and time. The components include nitrates, sulfates, elemental carbon, organic carbon compounds, acid aerosols, trace metals, and material from the earth's crust. Substances of biological origin, such as pollen and spores, may also be present.

Until several years ago, the health effects of particulates were focused on those sized 10 μm (micrometers) aerodynamic diameter and smaller. These can be inhaled through the upper airways and deposited in the lower airways and gas exchange tissues in the lung. These particles are referred to as PM10. EPA initially promulgated ambient air quality standards for PM10 of 150 $\mu g/m^3$ averaged over a 24-hour period, and 50 $\mu g/m^3$ for an annual average. EPA has since rescinded the annual PM10 standard, but kept the 24-hour standard.

In recent years additional focus has been placed on particles having an aerodynamic diameter of 2.5 μm or less (PM2.5). A greater faction of particles in this size range can penetrate and deposit deep in the lungs. The EPA recently lowered the air quality standards for PM2.5 to 35 $\mu g/m^3$ for a 24-hour average and reaffirmed 15 $\mu g/m^3$ for an annual average standard. There was considerable controversy and debate surrounding the review of particulate matter health effects and the consideration of ambient air quality standards (Kaiser, 1997; Vedal, 1997) when the EPA promulgated the initial PM2.5 standards in 1997.

Since that time, numerous studies have been published, and some of the key studies were closely scrutinized and analyses repeated. The result is that there are now substantial data confirming the adverse health effects of PM2.5 exposures.

There are also differences in the composition and sources of particles in the different size ranges that may have implications for health effects. The particles larger than 2.5 μm (often referred to as the coarse fraction) are mostly produced by mechanical processes. These include automobile tire wear, industrial processes such as cutting and grinding, and resuspension of particles from the ground or road surfaces by wind and human activities.

In contrast, particles smaller than 2.5 μm are mostly derived from combustion sources, such as automobiles, trucks, and other vehicle exhaust, as well as from stationary combustion sources. The particles are either directly emitted or are formed

in the atmosphere from gases that are emitted. Components from material in the earth's crust, such as dust, are also present, with the amount varying in different locations.

Attention to another range of very small particles has been increasing over the last few years. These are generally referred to as "ultrafine" particles, with diameters of 0.1 μm or less. These particles are mainly from fresh emissions of combustion sources, but are also formed in the atmosphere from photochemical reactions. Ultrafine particles have relatively short half lives (minutes to hours) and rapidly grow through condensation and coagulation process into larger particles within the PM2.5 size range. These particles are garnering interest since laboratory studies indicate that their toxicity may be higher on a mass basis than larger particles, and there is evidence that these small particles can translocate from the lung to the blood and to other organs of the body.

There have been several reviews of the health effects of ambient particulate matter (ATS, 1996; Brunekreef, 2002; U.S. EPA, 2004; U.S. EPA, 2009). In addition, the California Air Resources Board (CARB) and the Office of Environmental Health and Hazard Assessment (OEHHA) have reviewed the adequacy of the California Air Quality Standards for Particulate Matter (Cal EPA, 2002).

The major types of effects associated with particulate matter include:

- Increased mortality
- Exacerbation of respiratory disease and of cardiovascular disease as evidenced by increases in:
    - -Respiratory symptoms
    - -Hospital admissions and emergency room visits
    - -Physician office visits
    - -School absences
    - -Work loss days
- Effects on lung function
- Changes in lung morphology

The current federal and California standards are listed below:

TABLE I-4

Ambient Air Quality Standards for Particulate Matter

STANDARD	FEDERAL	CALIFORNIA
PM10 24-Hour average	150 μg/m^3	50 μg/m^3
PM10 Annual Average	--	20 μg/m^3
PM 2.5 24-Hour Average	35 μg/m^3	--
PM 2.5 Annual Average	15 μg/m^3	12 μg/m^3

Short-Term Exposure Effects

Epidemiological studies have provided evidence for most of the effects listed above. An association between increased daily or several-day-average concentrations of PM10 and excess mortality and morbidity is consistently reported from studies involving communities across the U.S. as well as in Europe, Asia, and South America. A review and analysis of epidemiological literature for acute adverse effects of particulate matter was published by the American Thoracic Society in 1996. Several adverse effects were listed as associated with daily PM10 exposures, as listed in Table I-5.~~undertaken by Dockery and Pope to estimate these effects as percent increase in mortality associated with each incremental increase of PM10 by 10 μg/m^3. The estimates are presented in Table I-5.~~ It also appears that individuals who are elderly or have preexistent lung or heart disease are more susceptible than others to the adverse effects of PM10 (ATS, 1996). Since then m~~M~~any more recent studies have confirmed that excess mortality and morbidity are associated with short term particulate matter levels (Pope, 2006).

Estimates of mortality effects from ~~these~~ studies of PM10 exposures range from 0.3 to 1.7% increase for a 10 μg/m^3 increase in PM10 levels. The National Morbidity, Mortality, and Air Pollution Study (NMMAPS), a study of 20 of the largest U.S. cities, determined a combined risk estimate of about a 0.5% increase in total mortality for a 10 μg/m^3 increase in PM10 (Samet, 2000a). This study also analyzed the effects of gaseous co-pollutants. The results indicated that the association of PM10 and mortality were not confounded by the presence of the gaseous pollutants. When the gaseous pollutants were included in the analyses, the significance of the PM10 estimates remained. The PM10 effects were reduced somewhat when O_3 was also considered and tended to be variably decreased when NO_2, CO, and SO_2 were

added to the analysis. These results argue that the effects are likely due to the particulate exposures; they cannot readily be explained by coexisting weather stresses or other pollutants.

An expansion of the NMMAPS study to 90 U.S. Cities also reported association with PM10 levels and mortality (Samet 2000b). It was discovered that this study was one that used a flawed statistical software package. The investigators have reanalyzed the data using corrected settings for the software (Dominici, 2002a, Dominici 2002b). When the estimates for the 90 cities in the study were recalculated, the estimate changed from 0.41% increase in mortality for a 10 $\mu g/m^3$ increase in PM10 to a 0.27% increase. There remained a strong positive association between acute exposure to PM10 and mortality. Thus while the quantitative estimate was reduced, the major findings of the study did not change.

TABLE I-5

Combined Effect Estimates of Daily Mean Particulate Pollution (PM10)

	% CHANGE IN HEALTH INDICATOR PER EACH 10 $\mu g/m^3$ INCREASE IN PM10
Increase in Daily Mortality	
Total deaths	1.0
Respiratory deaths	3.4
Cardiovascular deaths	1.4
Increase in Hospital Usage (all respiratory diagnoses)	
Admissions	1.4
Emergency department visits	0.9
Exacerbation of Asthma	
Asthmatic attacks	3.0
Bronchodilator use	12.2
Emergency department visits*	3.4
Hospital admissions	1.9
Increase in Respiratory Symptom Reports	
Lower respiratory	3.0
Upper respiratory	0.7

TABLE I-5 (concluded)

Combined Effect Estimates of Daily Mean Particulate Pollution

	% CHANGE IN HEALTH INDICATOR PER EACH 10 μg/m^3 INCREASE IN PM10
Cough	2.5
Decrease in Lung Function	
Forced expiratory volume	0.15
Peak expiratory flow	0.08

* One study only

(Source: American Journal of Respiratory and Critical Care Medicine, Vol. 153, 113-50, 1996)

Studies of PM2.5 also find associations with elevated mortality. The estimates for PM2.5 generally are in the range of 2.0 to 8.5% increase in total deaths per 25 μg/m^3 increase in 24-hour PM2.5 levels. The estimates for cardiovascular related mortality range from 3.0 to 7.0% per 25 μg/m^3 24-hour PM2.5, and for respiratory mortality estimates range from 2.0 to 7.0% per 25 μg/m^3 24-hour PM2.5.

Several studies have attempted to assess the relative importance of particles smaller than 2.5 μm and those between 2.5 μm and 10 μm (PM10-2.5). While some studies report that PM2.5 levels are better predictors of mortality effects, others suggest that PM10-2.5 is also important. Most of the studies found higher mortality associated with PM2.5 levels than with PM10-2.5. For example, a study of six cities in the U.S. found that particulate matter less than 2.5 μm was associated with increased mortality, but that the larger particles were not. Other studies in Mexico City and Santiago, Chile reported that PM10-2.5 was as important as PM2.5. Overall effects estimates for PM10-2.5 fall in the range of 0.5 to 6.0 % excess mortality per 25 μg/m^3 24-hour average.

The relative importance of both PM2.5 and PM10-2.5 may vary in different regions depending on the relative concentrations and components, which can also vary by season. More research is needed to better assess the relative effects of fine (PM2.5) and coarse (PM10-2.5) fractions of particulate matter on mortality.

A number of studies have evaluated the association between particulate matter exposure and indices of morbidity such as hospital admissions, emergency room

visits or physician office visits for respiratory and cardiovascular diseases. The effects estimates are generally higher than the effects for mortality. The effects are associated with measures of PM10 and PM2.5. Effects are also associated with PM10-2.5. Thus, it appears that when a relatively small number of people experience severe effects, larger numbers experience milder effects, which may relate either to the coarse or to the fine fraction of airborne particulate matter.

In the NMMAPS study, hospital admissions for those 65 years or older were assessed in 14 cities. Hospital admissions for these individuals showed an increase of 6% for cardiovascular diseases and a 10% increase for respiratory disease admissions, per 50 $\mu g/m^3$ increase in PM10. The excess risk for cardiovascular disease ranges from 3-10% per 50 $\mu g/m^3$ PM10 and from 4-10% per 25 $\mu g/m^3$ PM2.5 or PM10-2.5.

Similarly, school absences, lost workdays and restricted activity days have also been used in some studies as indirect indicators of acute respiratory conditions. The results are suggestive of both immediate and delayed impact on these parameters following elevated particulate matter exposures. These observations are consistent with the hypothesis that increased susceptibility to infection follows particulate matter exposures.

Some studies have reported that short-term particulate matter exposure is associated with changes in lung function (lung capacity and breathing volume); upper respiratory symptoms (hoarseness and sore throat); and lower respiratory symptoms (increased sputum, chest pain and wheeze). The severity of these effects is widely varied and is dependent on the population studied, such as adults or children with and without asthma. Sensitive individuals, such as those with asthma or pre-existing respiratory disease, may have increased or aggravated symptoms associated with short-term particulate matter exposures. Several studies have followed the number of medical visits associated with pollutant exposures. A range of increases from 3% to 42% for medical visits for respiratory illnesses was found corresponding to a 50 $\mu g/m^3$ change in PM10. A limited number of studies also looked at levels of PM2.5 or PM10-2.5. The findings suggest that both the fine and coarse fractions may have associations with some respiratory symptoms.

The biological mechanisms by which particulate matter can produce health effects are being investigated in laboratory studies. Inflammatory responses in the respiratory system in humans and animals exposed to concentrated ambient particles have been measured. These include effects such as increases in neutrophils in the lungs. Other changes reported include increased release of cytokines and interleukins,

chemicals released as part of the inflammatory process. The effects of particulate matter may be mediated in part through the production of reactive oxygen species during the inflammatory process. Recent reviews discuss mechanistic studies in more detail (Brunekreef, 2002; Brook, 2004).

Long-Term Exposure Effects

While most studies have evaluated the acute effects, some studies specifically focused on evaluating the effects of chronic exposure to PM10 and PM2.5. Studies have analyzed the mortality of adults living in different U.S. cities. After adjusting for important risk factors, taken as a whole these studies found a positive association of deaths and exposure to particulate matter. A similar association was observable in both total number of deaths and deaths due to specific causes. The largest effects were observed from cardiovascular causes and ischemic heart disease. A shortening of lifespan was also reported in these studies.

Since the initial promulgation by EPA of the National Ambient Air Quality Standards for PM2.5, controversy has remained over the association of mortality and exposures to PM2.5. Thus an expanded discussion of these studies is presented below.

Significant associations for PM2.5 for both total mortality and cardiorespiratory mortality were reported in a study following a national cohort recruited by the American Cancer Society for a Cancer Preventions Study over several years. A re-analysis of the data from this study confirmed the initial finding (Krewski, 2000). In this study, mortality rates and PM2.5 levels were analyzed for 51 metropolitan areas of the U.S. Average levels from monitors in each area were used to estimate exposures. At these levels of aggregation, regional differences in the association of PM2.5 and mortality were noted, with higher associations in the Northeast, and lower or non-significant associations in the West.

The Harvard Six Cities Study evaluated several size ranges of particulate matter and reported significant associations with PM15, PM2.5, sulfates, and non-sulfate particles, but not with coarse particles (PM15 – PM2.5). An extension of the Harvard Six Cities Cohort confirmed the association of mortality with PM2.5 levels (Laden, 2006). These studies provide evidence that the fine particles, as measured by PM2.5, may be more strongly associated with mortality effects from long-term particulate matter exposures than are coarse compounds. An update to this study covering a follow-up over the years 1974 to 2009 (Lepeule, 2012) was recently published. Findings indicated a linear relationship of PM2.5 levels and mortality

from all causes, cardiovascular causes, and from lung cancer. According to the authors, the PM2.5 levels decreased over time, but no evidence of a threshold for these effects was found.

A follow-up study of the American Cancer Society cohort confirmed and extended the findings in the initial study. The researchers estimated that, on average, a 10 ug/m3 increase in fine particulates was associated with approximately a 4% increase in total mortality, a 6% increase in cardiopulmonary mortality, and an 8% increase risk of lung cancer mortality (Pope, 2002). The magnitude of effects is larger in the long-term studies than in the short-term investigations. In an additional re analysis and extension of the American Cancer Society cohort from 1982 to 2000 (Krewski, 2009), and including additional metropolitan areas for the most recent years, effects estimates on mortality were similar, though somewhat higher, than those reported previously.

Other national studies include an analysis of mortality and PM2.5 exposures in a Medicare population. Zeger and Associates (2008) assembled a Medicare cohort by including all Medicare enrollees residing in zip codes with centroids within 6 miles of a PM2.5 monitor. PM2.5 data was obtained from the monitoring stations, and mean annual levels were called for the zip codes within six miles of each monitor. The estimated associations between exposures to PM2.5 and mortality for the eastern and central portions of the U.S were similar to those previously published in the Six Cities Study and the American Cancer Society cohorts. The authors reported that there were no significant associations between zip code levels of PM2.5 and mortality rates in the western region of the U.S. This lack of association was attributed largely to the higher PM2.5 levels in Los Angeles area counties compared to other western urban areas, but there were not higher mortality rates in these counties. The authors further reported that they found no associations of PM2.5 with mortality in persons aged 85 years or higher.

Analyses of mortality and PM2.5 levels specific to California have also been reported. A cohort of elderly individuals (average age of 65 yr in 1973) recruited from 11 California counties was followed over several years (Enstrom, 2005). An association for exposure with all cause deaths was reported from 1973–1982. However, no significant association was found in the later time period of 1983–2002. Pollutant levels were taken from ambient monitors and averaged over each county to estimate exposures.

Two analyses of the American Cancer Society cohort focused specifically on the Los Angeles Metropolitan area using methods to estimate exposures on a finer geographical scale than previous studies that used geographic scales at the county or metropolitan area. Using data from monitoring stations in the Los Angeles area, one study applied interpolation methods (Jerrett, 2005) and another applied land use regression techniques (Krewski, 2009) to estimate exposures to the study individuals. Significant associations of PM2.5 with mortality from all causes and cardiopulmonary disease were reported, with the magnitude of risks being up to three times higher than those from the national studies of the American Cancer Society cohort. This provides evidence that using methods to provide more detailed exposure estimates can result in stronger associations of PM2.5 and mortality.

Two recent reports have been released looking at air pollution and health effects in California. One study (Lipsett, 2011) followed school teachers recruited in 1995, and followed through 2005. Pollutant exposures at the subject residence were estimated using data from ambient monitors, and extrapolated using a distance weighted method. The authors reported significant association of PM2.5 levels and mortality from ischemic heart disease, but no associations were found with all cause, cardiovascular, or respiratory disease.

The second study (Jerrett, 2011) followed individuals in ~~the Los Angeles area~~ California from the American Cancer Society cohort recruited starting in 1982, with follow up to 2000. Pollutant levels at subject residences were estimated using several methods. All but one of the methods found no association of all-cause mortality with PM2.5 levels. All exposure estimation methods were reported to have found significant associations with ischemic heart disease mortality, however. The authors noted that mortality rates differ in urban areas compared to non-urban areas, and so included a variable for this in a land use regression model to estimate effects on mortality. When the authors applied the land use regression model including an urban indicator to estimate exposures, all-cause mortality, mortality from cardiovascular disease, and mortality from ischemic heart disease were all significantly associated with PM2.5 levels.

The U.S. EPA has recently proposed to lower the annual National Ambient Air Quality Standard for PM2.5 (U.S. EPA, 2012a). EPA also released a Regulatory Impact Analysis (U.S. EPA 2012b)which looked at the costs and benefits of alternate PM2.5 stand levels. As part of the analysis, EPA also looked at California specific studies regarding PM2.5 and mortality published in the scientific literature. The EPA

analysis concluded "most of the cohort studies conducted in California report central effect estimates similar to the (nation-wide) all-cause mortality risk estimate we applied from Krewski et al. (2009) and Laden et al. (2006) albeit with wider confidence intervals. A couple cohort studies conducted in California indicate higher risks than the risk estimates we applied." Thus in EPAs judgment the California related studies provided estimates of mortality consistent with or higher than those from the national studies.

Other studies report evidence indicating that particulate matter exposure early in pregnancy may be associated with lowered birth weights (Bobak, 1999). Studies from the U.S., the Czech Republic and Mexico City have reported that neonatal and early postnatal exposure to particulate matter may lead to increased infant mortality. A more recent study in Southern California found increased risks for infant deaths associated with exposures to particulates and other pollutants (Ritz, 2006). These results suggest that infants may be a subgroup affected by particulate matter exposures.

In addition, some long-term effect studies have reported an increased risk of mortality from lung cancer associated with particulate matter exposures. A study involving California Seventh Day Adventists (very few of whom smoke) has reported an association of lung cancer mortality with PM10 levels. It is not clear from these studies whether the association relates to causation of disease, or whether individuals with cancer are more susceptible to other effects of particles leading to the observed mortality association. A study that followed a large number of individuals living in the largest U.S. cities found elevated lung cancer risk associated with long-term average PM2.5 levels (Pope, 2002).

Several studies have assessed the effects of long-term particulate matter exposure on respiratory symptoms and lung function changes. Associations have been found with symptoms of chronic bronchitis and decreased lung function. A study of school children in 12 communities in Southern California showed significant association of particulate matter with bronchitis or phlegm in children with asthma. These effects were also associated with NO_2 and acid vapor levels.

A cohort of fourth graders from the Southern California communities was followed over a period of four years by the Children's Health Study. A lower rate of growth in lung function was found in children living in areas with higher levels of particulate pollution (Gauderman, 2000). Decreases in lung function growth were associated with PM10, PM2.5, PM10-2.5, acid vapor, and NO_2. There was no association with

ozone levels. The investigators were not able to identify independent effects of the pollutants, but noted that motor vehicle emissions are a major source of the pollutants.

A follow-up study on a second cohort of children confirmed the findings that decreased lung function growth was associated with particulates, nitric oxides, and elemental carbon levels (Gauderman, 2002). Elemental carbon is often used as a measure for diesel particulate. Additionally, children who moved to areas with less air pollution were found to regain some of the lung function growth rate (Avol, 2001). By the time the fourth graders graduated from high school, a significant number showed lower lung function. The risk of lower lung function was about five times higher in children with the highest PM2.5 exposure when compared to the lowest exposure communities (Gauderman, 2004). These deficits are likely to persist since the children were at the end of their growth period.

Despite data gaps, the extensive body of epidemiological studies has both qualitative and quantitative consistency suggestive of causality. A considerable body of evidence from these studies suggests that ambient particulate matter, alone or in combination with other coexisting pollutants, is associated with significant increases in mortality and morbidity in a community.

In summary, the scientific literature indicates that an increased risk of mortality and morbidity is associated with particulate matter at ambient levels. The evidence for particulate matter effects is mostly derived from population studies with supportive evidence from clinical and animal studies. Although most of the effects are attributable to particulate matter, co-pollutant effects cannot be ruled out on the basis of existing studies. The difficulty of separating the effects may be due to the fact that particulate levels co-vary with other combustion source pollutants. That is, the particle measurements serve as an index of overall exposure to combustion-related pollution, and some component(s) of combustion pollution other than particles might be at least partly responsible for the observed health effects.

EPA staff has presented conclusions on causal determination of several health effects based on a recent review of the available scientific studies (EPA, 2009). These are depicted in the Table below.

TABLE I-6

Summary of Causal Determination of PM2.5 by Exposure Duration and Health Outcome

SHORT-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular effects	Causal
Respiratory effects	Likely to be causal
Central nervous system	Inadequate information to assess
Mortality	Causal
LONG-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular effects	Causal
Respiratory effects	Likely to be causal
Mortality	Causal
Reproductive and developmental	Suggestive of a causal relationship
Cancer, Mutagenicity, Genotoxicity	Suggestive of a causal relationship

From EPA, 2009

ULTRAFINE PARTICLES

As noted above, numerous studies have found association of particulate matter levels with adverse effects, including mortality, hospital admissions, and respiratory disease symptoms. The vast majority of these studies used particle mass of PM10 or PM2.5 as the measure of exposure. Some researchers have postulated, however, that ultrafine particles may be responsible for some of the observed associations of particulate matter and health outcomes (Oberdorster, et al, 1995; Seaton, et al, 1995). Ultrafine particles are generally classified of 0.1 μm and small diameter.

Several potential mechanisms have been brought forward to suggest that the ultrafine portion may be important in determining the toxicity of ambient particulates, some of which are discussed below.

For a given mass concentration, ultrafine particles have much higher numbers and surface area compared to larger particles. Particles can act as carriers for other adsorbed agents, such as trace metals and organic compounds; and the larger surface area may transport more of such toxic agents than larger particles.

Smaller particles can also be inhaled deep into the lungs. As much as 50% of 0.02 µm diameter particles are estimated to be deposited in the alveolar region of the lung. There is complex nature of the relation between deposition and particle size. The ultrafine particles generally have higher fractional deposition in the alveolar region. However, for the smaller nucleation mode (particles less than 0.01 µm size) the deposition in the alveolar region declines, but increases in the extrathoracic region.

Exposures of laboratory animals to ultrafine particles have found cardiovascular and respiratory effects. Mice exposed to concentrated near roadway ultrafine particles showed larger early atherosclerotic lesions than mice exposed to PM2.5 or filtered air (Arujo, 2008). In a mouse allergy model, exposures to concentrated ultrafine particles resulted in a greater response to antigen challenge to ovalbumin (Li, 2010), indicating that vehicular traffic exposure could exacerbate allergic inflammation in already-sensitized animals.

Controlled exposures of human volunteers to ultrafine particles either laboratory generated or as products of combustion, such as diesel exhaust containing particles, have found physiological changes related to vascular effects. Mills, 2011, for example found exposure to diesel exhaust particulate attenuated both acetylcholine and sodium-nitroprusside -induced vasorelaxation.

There are no long-term studies of human population exposure to ultrafine particle, as there is a lack of a monitoring network in the U.S. There have been several cross sectional epidemiological studies of ultrafine particles, mainly from Europe. Some of these studies found effects on hospital admissions, emergency department visits, for respiratory and cardiovascular effects. Other studies, however, have not found such effects (EPA, 2009). Concentrations of ultrafine particles can vary geographically, and it is not clear how well central site monitors may capture actual exposures.

EPA staff has presented conclusions on causal determination of several health effects of ultrafine PM based on a recent review of the available scientific studies (EPA, 2009). These are depicted in the table below.

Additional discussion on the sources and health effects of ultrafine particles can be found in Chapter 9 of the 2012 AQMP.

TABLE I-7

Summary of Causal Determination of Ultrafine PM by Exposure Duration and Health Outcome

SHORT-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular effects	Suggestive
Respiratory effects	Suggestive
Central nervous system	Inadequate information to assess
Mortality	Inadequate
LONG-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular effects	Inadequate
Respiratory effects	Inadequate
Mortality	Inadequate
Reproductive and developmental	Inadequate
Cancer, Mutagenicity, Genotoxicity	Inadequate

From EPA, 2009

CARBON MONOXIDE

The high affinity of carbon monoxide (CO) to bond with oxygen-carrying proteins (hemoglobin and myoglobin) results in reduced oxygen supply in the bloodstream of exposed individuals. The reduced oxygen supply is responsible for the toxic effects of CO which are typically manifested in the oxygen-sensitive organ systems. The effects have been studied in controlled laboratory environments involving exposure of humans and animals to CO, as well as in population-based studies of ambient CO exposure effects. People with deficient blood supply to the heart (ischemic heart disease) are known to be susceptible to the effects of CO. Protection of this group is the basis of the existing National Ambient Air Quality Standards for CO at 35 ppm for one hour and 9 ppm averaged over eight hours. The health effects of ambient CO have been recently reviewed (U.S. EPA, 2000, 2010).

Inhaled CO has no known direct toxic effect on lungs but rather exerts its effects by interfering with oxygen transport through the formation of carboxyhemoglobin (COHb, a chemical complex of CO and hemoglobin). Exposure to CO is often evaluated in terms of COHb levels in blood measured as percentage of total hemoglobin bound to CO. COHb levels in non-smokers range between 0.3 and 0.7% and 5 to 10% in smokers. COHb levels in excess of 1.5% in a significant proportion of urban non-smoking populations can be considered as evidence of widespread exposure to environmental CO.

Under controlled laboratory conditions, healthy subjects exposed to CO sufficient to result in 5% COHb levels exhibited reduced duration of maximal exercise performance and consumption of oxygen. Studies involving subjects with coronary artery disease who engaged in exercise during CO exposures have shown that COHb levels as low as 2.4% can lead to earlier onset of electrocardiograph changes indicative of deficiency of oxygen supply to the heart. Other effects include an earlier onset of chest pain, an increase in the duration of chest pain, and a decrease in oxygen consumption.

Findings of epidemiologic studies have observed associations between ambient CO concentration and emergency department visits and hospital emissions for ischemic heart disease and other cardiovascular diseases.

Animal studies associated with long-term exposure to CO resulting in COHb levels that are equivalent to those observed in smokers have shown indication of reduction in birth weight and impaired neurobehavior in the offspring of exposed animals.

Epidemiological studies conducted in Southern California have indicated an association with CO exposure during pregnancy to increases in pre-term births. (Ritz, 2000). However, the results were not consistent in different areas studied. The increase in the pre-term births was also associated with PM10 levels. Another study found increased risks for cardiac related birth defects with carbon monoxide exposure in the second month of pregnancy (Ritz, 2002). Toxicological studies in laboratory animals with higher than ambient levels of CO have also reported decrements in birth weight and prenatal growth.

EPA staff has presented conclusions on causal determination of the health effects of carbon monoxide based on a recent review of the available scientific studies (EPA, 2010). These are depicted in the table below.

TABLE I-8

Causal Determination for Health Effects of Carbon Monoxide

SHORT-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular morbidity	Likely to be a causal relationship
Central nervous system	Suggestive
Respiratory morbidity	Suggestive
Mortality	Suggestive
LONG-TERM EXPOSURES	
Health Outcome	**Causality Determination**
Cardiovascular morbidity	Inadequate
Central nervous system	Suggestive
Birth outcomes and developmental effects	Suggestive
Respiratory morbidity	Inadequate
Mortality	Not likely to be a causal relationship

From EPA, 2010

NITROGEN DIOXIDE

The U.S. EPA has recently reviewed the health effects of nitrogen dioxide (U.S. EPA, 2008a). Evidence for low-level nitrogen dioxide (NO_2) exposure effects is derived from laboratory studies of asthmatics and from epidemiological studies. Additional supportive evidence is derived from animal studies.

Epidemiological studies using the presence of an unvented gas stove as a surrogate for indoor NO_2 exposures suggest an increased incidence of respiratory infections or symptoms in children.

Recent studies related to outdoor exposure have found health effects associated with ambient NO_2 levels, including respiratory symptoms, respiratory illness, decreased lung function, increased emergency room visits for asthma, and cardiopulmonary mortality. However, since NO_2 exposure generally occurs in the presence of other pollutants, such as particulate matter, these studies are often unable to determine the specific role of NO_2 in causing effects.

The Children's Health Study in Southern California found associations of air pollution, including NO_2, PM10, and PM2.5, with respiratory symptoms in asthmatics (McConnell, 1999). Particles and NO_2 were correlated, and effects of individual pollutants could not be discerned. A subsequent analysis indicated a stronger role for NO2 (McConnell, 2002).

Ambient levels of NO_2 were also associated with a decrease in lung function growth in a group of children followed for eight years. In addition to NO_2, the decreased growth was also associated with particulate matter and airborne acids. The study authors postulated that these may be a measure of a package of pollutants from traffic sources. (Gauderman, 2004).

Results from controlled exposure studies of asthmatics demonstrate an increase in the tendency of airways to contract in response to a chemical stimulus (bronchial reactivity). Effects were observed with exposures from 0.1 to 0.3 ppm NO_2 for periods ranging from 30 minutes to 3 hours. A similar response is reported in some studies with healthy subjects at higher levels of exposure (1.5 - 2.0 ppm). Mixed results have been reported when people with chronic obstructive lung disease are exposed to low levels of NO_2.

Short-term controlled studies of animals exposed to NO_2 over a period of several hours indicate cellular changes associated with allergic and inflammatory response and interference with detoxification processes in the liver. In some animal studies

the severity of the lung structural damage observed after relatively high levels of short-term ozone exposure is observed to increase when animals are exposed to a combination of ozone and NO_2.

In animals, longer-term (3-6 months) repeated exposures at 0.25 ppm appear to decrease one of the essential cell-types (T-cells) of the immune system. Non-specific changes in cells involved in maintaining immune functions (cytotoxic T-cells and natural killer cells) have been observed in humans after repeated exposure (4-6 days) to >0.6 ppm of NO_2 (20 min. - 2 hours). All these changes collectively support the observation reported both in population and animal studies of increased susceptibility to infections, as a result of NO_2 exposure.

The U.S. EPA recently adopted a new short-term standard of 100 ppb (0.1 ppm) averaged over 1 hour. The standard was designed to protect against increases in airway reactivity in individuals with asthma observed in controlled exposure studies, as well as respiratory symptoms observed in epidemiological studies.

SULFUR DIOXIDE

Controlled laboratory studies involving human volunteers have clearly identified asthmatics as the most sensitive group to the effects of ambient sulfur dioxide ($SO_{2)}$ exposures. Healthy subjects have failed to demonstrate any short-term respiratory functional changes at exposure levels up to 1.0 ppm over 1-3 hours.

In exercising asthmatics, brief exposure (5-10 minutes) to SO_2 at levels between 0.2-0.6 ppm can result in significant alteration of lung function, such as increases in airway resistance and decreases in breathing capacity. In some, the exposure can result in severe symptoms necessitating the use of medication for relief. The response to SO_2 inhalation is observable within 2 minutes of exposure, increases further with continuing exposure up to 5 minutes then remains relatively steady as exposure continues. SO_2 exposure is generally not associated with any delayed reactions or repetitive asthmatic attacks.

In epidemiologic studies, associations of SO_2 levels with increases in respiratory symptoms, increases in emergency department visits and hospital admissions for respiratory-related causes have been reported.

The U.S. EPA has recently revised the SO_2 air quality standard. The previous 24-hour standard was rescinded and replaced with a new 1-hour standard at 75 ppb (0.075 ppm) to protect against high short-term exposures.

Animal studies have shown that despite SO_2 being a respiratory irritant, it does not cause substantial acute or chronic toxicity in animals exposed at ambient concentrations. However, relatively high exposures (10 ppm of SO_2 for 72 hours) in mice can lead to tissue damage, fluid accumulation and sloughing of respiratory lining. Sensitization to allergies is observable in guinea pigs repeatedly exposed to high levels (72 ppm) of SO_2. This effect needs further evaluation in clinical and population studies to identify any chronic exposure impact on both asthmatic incidence and attacks in a population.

Some epidemiological studies indicate that the mortality and morbidity effects associated with the fine fraction of particles show a similar association with ambient SO_2 levels. In these studies, efforts to separate the effects of SO_2 from fine particles have not been successful. Thus, it is not clear whether the two pollutants act synergistically, or whether being generated from similar combustion sources, they represent the same pollution index for the observed effects.

SULFATES

Based on a level determined necessary to protect the most sensitive individuals, the California Air Resources Board (CARB) in 1976 adopted a standard of 25 $\mu g/m^3$ (24-hour average) for sulfates. There is no federal air quality standard for sulfates.

In recent years, a vast majority of effects (mortality and morbidity) associated with fine particles (PM2.5) and sulfur dioxide have shown a similar association with ambient sulfate levels in some population studies. The efforts to fully separate the effects of sulfates from other coexisting pollutants have not been successful. This may be due to the fact that these pollutants covary under ambient conditions, having been emitted from common sources; and the effects observed may be due to the combination of pollutants, rather than a single pollutant.

A clinical study involving exposure of human subjects to sulfuric acid aerosol indicated that adolescent asthmatics may be a susceptible population subgroup with some changes in lung function observed with exposures below 100 $\mu g/m^3$. In general, however, laboratory exposures of human volunteers to sulfates at or near ambient levels have not found significant changes in lung function.

Results from animal studies involving exposures to sulfuric acid aerosol, ammonium bisulfate and ammonium sulfate indicate that acidic particles (former two) are more toxic than non-acidic particles (latter). In addition, the severity or magnitude of both

mortality and morbidity effects is relatively higher in population studies of the eastern United States and Canada where sulfate concentrations are higher than for those observed in the western United States. Mixed results have been reported from studies which attempted to ascertain the role of acidity in determining the observed toxicity.

LEAD

The U.S. EPA has recently reviewed the health effects of ambient lead exposures in conjunction with a review of the NAAQS for lead. (U.S. EPA 2006b; U.S. EPA 2007b). The following summary is taken from these reviews.

There are a number of potential public health effects at low level exposures. The health implications are generally indexed by blood lead levels, which are related to lead exposures both from inhalation as well as from ingestion. As identified by EPA, effects includeimpacts on population IQ, as well as heart disease and kidney disease. The array of health effects includes the following.

- Heme biosynthesis and related functions;
- Neurological development and function;
- Reproduction and physical development;
- Kidney function;
- Cardiovascular function
- Immune function

Children appear to be sensitive to the neurological toxicity of lead, with effects observed at blood lead concentration ranges of 5 – 10 µg/dL, or possibly lower. No clear threshold has yet been established for such effects.

According to the EPA review, the most important effects observed are neurotoxic effects in children and cardiovascular effects in adults. The effects in children include impacts on intellectual attainment and school performance.

EPA has recently revised the NAAQS for lead to a level of 0.15 µg/m^3 averaged over a 3 month period to protect against lead toxicity. The following two charts, taken from the U.S. EPA review, depict the health effects of lead in relation to blood levels.

Lowest Observed Effect Blood Lead Level	Neurological Effects	Hematological Effects	Immune Effects
30 µg/dL		Increased urinary δ-aminolevulinic acid	
15 µg/dL	Behavioral disturbances (e.g., inattention, delinquency) Altered electrophysiological responses	Erythrocyte protoporphyrin (EP) elevation	
10 µg/dL	Effects on neuromotor function CNS cognitive effects (e.g., IQ deficits)	Inhibition of δ-aminolevulinic acid dehydratase (ALAD) Pyrimidine-5′-nuclotidase (Py5N) activity inhibition	Effects on humoral (↑ serum IgE) and cell-mediated (↓ T-cell abundance) immunity
5 µg/dL	(???)	(???)	
0 µg/dL			

FIGURE I-2

Summary of Lowest Observed Effect Levels for Key Lead- Induced Health Effects in Children (From U.S. EPA 2007b)

Lowest Observed Effect Blood Lead Level	Neurological Effects	Hematological Effects	Cardiovascular Effects	Renal Effects
30 µg/dL	Peripheral sensory nerve impairment	Erythrocyte protoporphyrin (EP) elevation in males		Impaired Renal Tubular Function
20 µg/dL	Cognitive impairment			
15 µg/dL	Postural sway	Erythrocyte protoporphyrin (EP) elevation in females Increased urinary δ-aminolevulinic acid		
10 µg/dL		Inhibition of δ-aminolevulinic acid dehydratase (ALAD)	Elevated blood pressure	
5 µg/dL			(???)	Elevated serum creatine (↓ creatine clearance)
0 µg/dL				

FIGURE I-3

Summary of Lowest Observed Effect Levels for Key Lead- Induced Health Effects in Adults (From U.S. EPA 2007b)

TOXIC AIR CONTAMINANTS

Toxic air contaminants are pollutants for which there generally are no ambient air quality standards. Under California's Air Toxics Program, CARB staff and Office of Environmental Health Hazard Assessment (OEHHA) assess the health effects of substances that may pose a risk of adverse health effects. These effects are usually an increased risk for cancer or adverse birth outcome. After review by the state Scientific Review Panel, CARB holds a public hearing on whether to formally list substances that may pose a significant risk to public health as a Toxic Air Contaminant.

CARB and OEHHA also establish potency factors for air toxics that are carcinogenic. The potency factors can be used to estimate the additional cancer risk from ambient levels of toxics. This estimate represents the chance of contracting cancer in an individual over a lifetime exposure to a given level of an air toxic and is usually expressed in terms of additional cancer cases per million people exposed.

The District conducted studies on the ambient concentrations and estimated the potential health risks from air toxics (SCAQMD, 2008). In the latest study, a two year monitoring program was undertaken at 10 sites throughout the SCAB over the time period 2004-2006. Over 30 substances were measured, and annual average levels were calculated. The results showed that the overall risk for excess cancer from a 70-year lifetime exposure to the levels of air toxics calculated as the average level at the 10 sites was about 1,200 in a million. The largest contributor to this risk was diesel ~~exhaust~~particulate matter, accounting for about 84% of the air toxics risk. A breakdown of the major contributors to the air toxics risk is shown in ~~FIGURE I-2~~FIGURE I-4.

While the California Air Resources Board listed Diesel Particulate Matter as a Toxic Air Contaminant in 1989, the International Agency for Research on Cancer, an arm of the World Health Organization, recently convened an international panel of scientists to review the published literature regarding the carcinogenicity of diesel combustion emissions. The panel concluded that Diesel Exhaust is a substance that causes cancer in humans (Benbrahim-Tallaa, 2012).

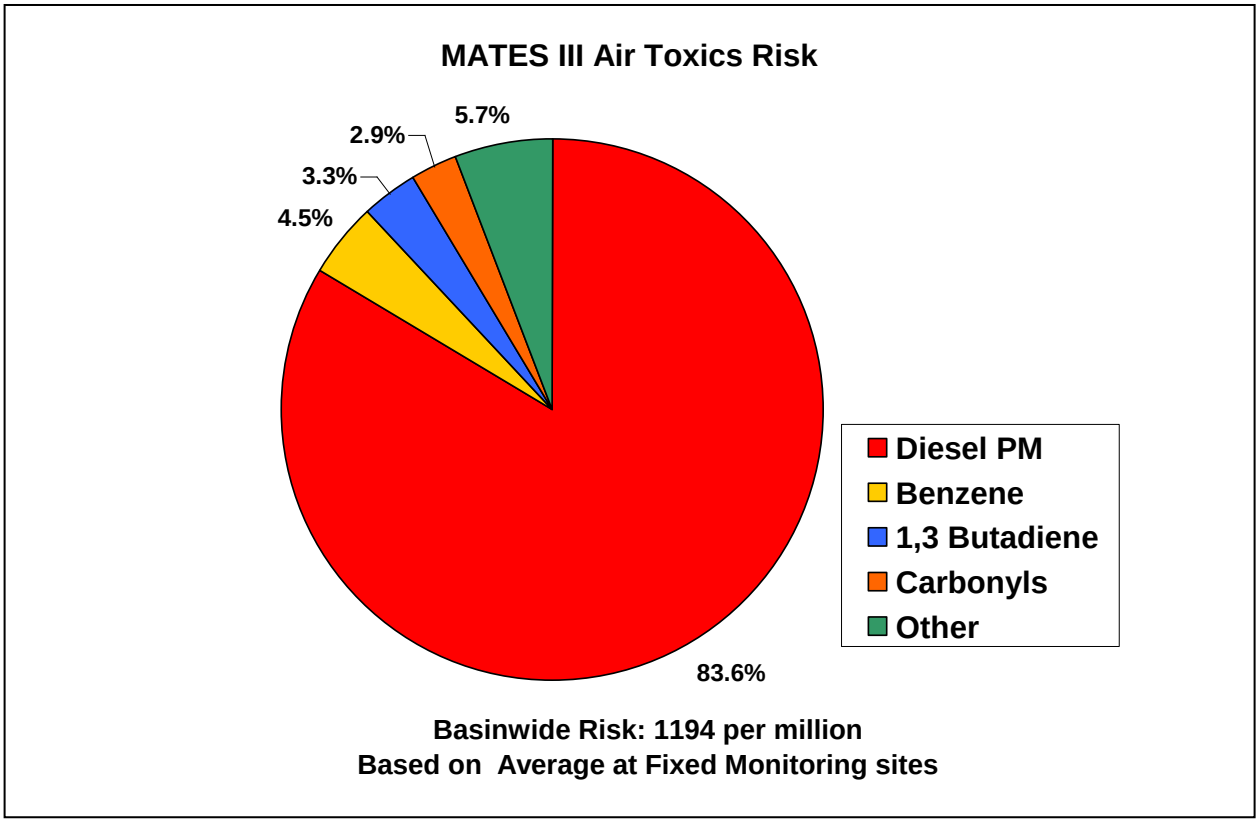

FIGURE I-4~~2~~

Major Pollutants Contributing to Air Toxics Cancer Risk in the South Coast Air Basin

For non-cancer health effects, OEHHA has developed acute and chronic Reference Exposure Levels (RELs). RELs are concentrations in the air below which adverse health effects are not likely to occur. Acute RELs refer to short-term exposures, generally of one-hour duration. Chronic RELs refer to long-term exposures of several years. The ratio of ambient concentration to the appropriate REL can be used to calculate a Hazard Index. A Hazard Index of less than one would not be expected to result in adverse effects. The measured levels from the most recent study were below the applicable Reference Exposure Levels.

The key air toxics contributing to risk from mobile and stationary sources are listed in TABLE I-9.

TABLE I-9

Key Toxic Air Contaminants in the SCAB

MOBILE SOURCES	STATIONARY SOURCES
Acetaldehyde	Hexavalent Chromium
Benzene	Methylene Chloride
1,3 Butadiene	Nickel
Diesel ~~Exhaust~~Particulate Matter	Perchloroethylene
Formaldehyde	Trichloroethylene

CONCLUSION

A large body of scientific evidence shows that the adverse impacts of air pollution in human and animal health are clear. A considerable number of population-based and laboratory studies have established a link between air pollution and increased morbidity and, in some instances, earlier mortality ~~and air pollution~~.

As the scientific methods for the study of air pollution health effects has progressed over the past decades, adverse effects have been shown to occur at lower levels of exposure. For some pollutants, no clear thresholds for effects have been demonstrated. The new findings have, in turn, led to the revision and lowering of National Ambient Air Quality Standards which, in the judgment of the Administrator of the U.S. EPA, are necessary to protect public health. The figures below are meant to convey some of the historical context to recent revisions to the NAAQS for ozone and for particulate matter.

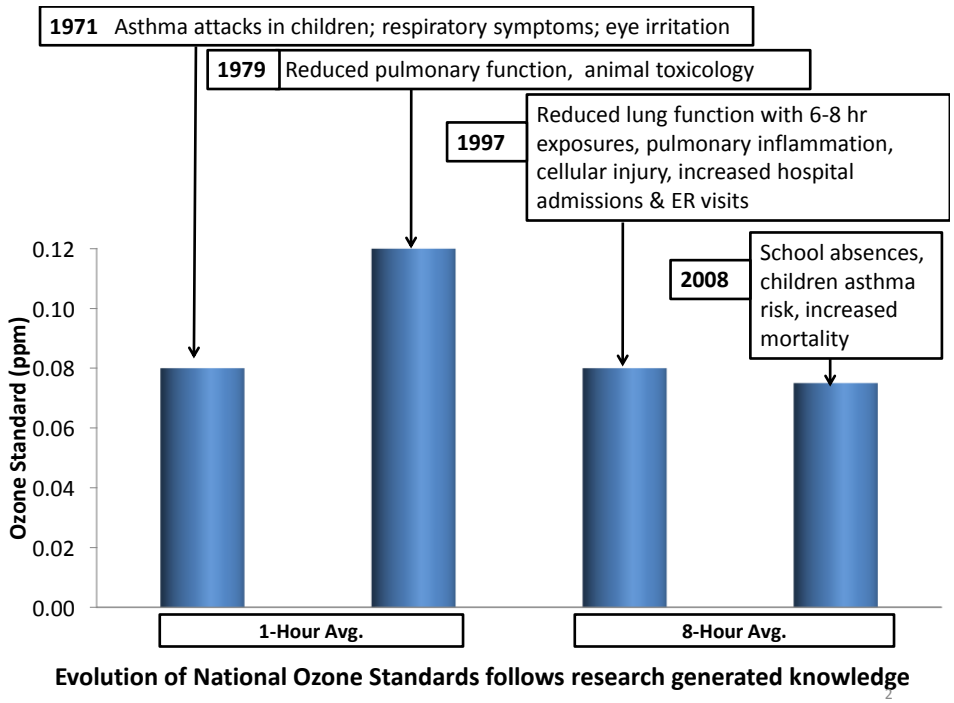

FIGURE I-4

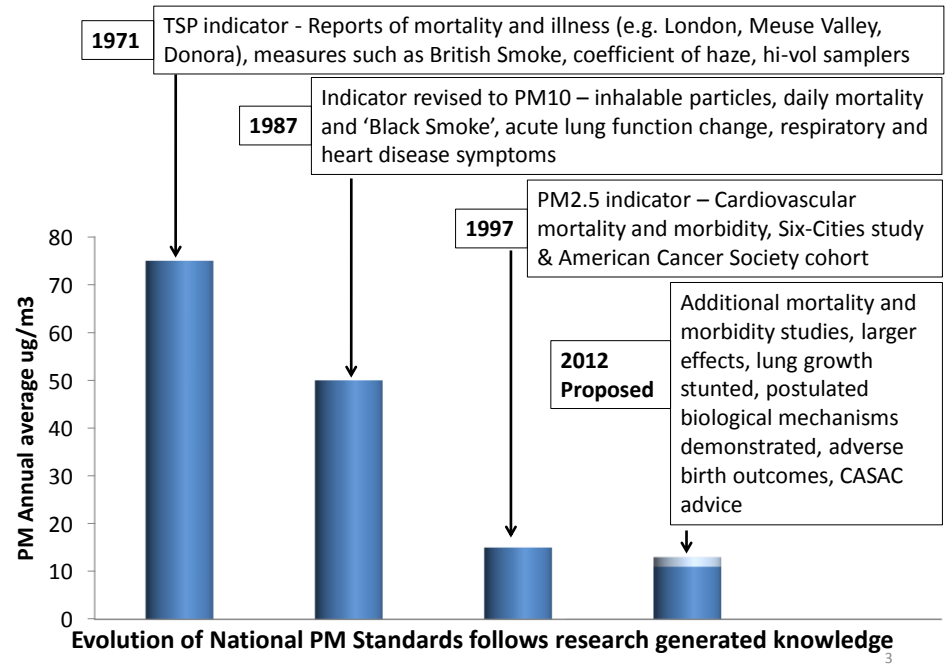

FIGURE I- 5

REFERENCES

American Thoracic Society, Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. (1996). "Health Effects of Outdoor Air Pollution." American Journal Respiratory and Critical Care Medicine, Parts 1 and 2. 153:3-50 and 153:477-498.

Araujo JA, Barajas B, Kleinman M, Wang X, Bennett BJ, Gong KW, Navab M, Harkema J, Sioutas C, Lusis AJ, Nel AE. (2008) Ambient particulate pollutants in the ultrafine range promote early atherosclerosis and systemic oxidative stress. Circ Res. 14;102(5):589-96.

Avol EL, Gauderman JW, Tan SM, London SJ, Peters JM. (2001). "Respiratory Effects of Relocating to Areas of Differing Air Pollution Levels." Am J Respir Crit Care Med, 164:11:2067-2072.

Benbrahim-Tallaa L, Baan RA, Grosse Y, Lauby-Secretan B, El Ghissassi F, Bouvard V, Guha N, Loomis D, Straif K, on behalf of the International Agency for Research on Cancer Monograph Working Group (2012). The Lancet Oncology, 13(7): 663-664

Bell ML, McDermott A, Zeger SL, Samet, JM, Dominici, F. (2004). "Ozone and Short-Term Mortality in 95 US Urban Communities, 1987-2000." JAMA 292:2372-2378.

Bell, ML; Dominici, F. (2008). Effect modification by community characteristics on the short-term effects of ozone exposure and mortality in 98 US communities. Am J Epidemiol 167: 986-997.

Bobak M, Leon DA. (1999). "Pregnancy Outcomes and Outdoor Air Pollution: An Ecological Study in Districts of the Czech Republic 1986-8." Occup. and Environ. Med. 56:539-543.

Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, Leupker R, Mittleman M, Samet J, Smith SC Jr., Tager I. (2004). "Air Pollution and Cardiovascular Disease: A Statement for Healthcare Professionals from the Expert Panel on Population and Prevention Science of the American Heart Association." Circulation, 109:2655-2671.

Brown JS, Bateson TF, McDonnell WF (2008). Effects of Exposure to 0.06 ppm Ozone on FEV1 in Humans: A Secondary Analysis of Existing Data. Environ Health Perspect 116:1023-1026.

Brunekreef, B and ST Holgate. (2002). "Air Pollution and Health." The Lancet, 360(9341):1233-42.

California Environmental Protection Agency, Air Resources Board. (2005). "Review of the California Ambient Air Quality Standard for Ozone."

California Environmental Protection Agency, California Air Resources Board, and Office of Environmental Health Hazard Assessment. (2002). "Public Hearing to Consider Amendments to the Ambient Air Quality Standards for Particulate Matter and Sulfates." http://arbis.arb.ca.gov/research/aaqs/std-rs/pm-final/pm-final.htm#Summary.

California Environmental Protection Agency, California Air Resources Board and Office of Health Hazard Assessment. (2006). "Review of the California Ambient Air Quality Standard for Nitrogen Dioxide." Draft Staff Report.

Dominici F, McDermott A, Zeger SL, Samet JM. (2002). A Report to the Health Effects Institute: Reanalyses of the NMMAPS Database.

Dominici F, McDermott A, Zeger SL, Samet JM. (2002.) "On the use of Generalized Additive Models in Time-Series Studies of Air Pollution and Health." Am J Epidemiol., 156:193-203.

Gauderman JW, Avol E, Gilliland F, Vora H, Thomas D, Berhane K, McConnell R, Kuenzli N, Lurmann F, Rappaport E, Margolis H, Bates D, Peters J. (2004). "The Effect of Air Pollution on Lung Development from 10 to 18 Years of Age." N Engl J Med, 351(11):1057-1067.

Gauderman JW, Gilliland F, Vora H, Avol E, Stram D, McConnell R, Thomas D, Lurmann F, Margolis HG, Rappaport EB, Berhane K, Peters J. (2002). "Association between Air Pollution and Lung Function Growth in Southern California Children. Results from a Second Cohort." Am J Respir Crit Care Med, 166:76-84.

Gauderman JW, McConnell R, Gilliland F, London S, Thomas D, Avol E, Vora H, Berhane K, Rappaport EB, Lurmann F, Margolis HG, Peters J. (2000). "Association between Air Pollution and Lung Function Growth in Southern California Children." Am J Respir Crit Care Med, 162(4):1383-1390.

Gilliland FD, Berhane K, Rappaport EB, Thomas DC, Avol E, Gauderman WJ, London SJ, Margolis HG, McConnell R, Islam KT, Peters JM. (2001). "The Effects of Ambient Air Pollution on School Absenteeism Due to Respiratory Illnesses." Epidemiology, 12(1):43-54.

Jerrett M, Burnett RT, Ma R, Pope CA III, Krewski D, Newbold KB, Thurston G, Shi Y, Finkelstein N, Calle EE, Thun MJ. (2005). "Spatial Analysis of Air Pollution and Mortality in Los Angeles. Epidemiology, 15(6):727-736.

Jerrett, M; Burnett, RT; Pope, CA, III; Ito, K; Thurston, G; Krewski, D; Shi, Y; Calle, E; Thun, M. (2009). Long-term ozone exposure and mortality. N Engl J Med 360: 1085-1095.

Krewski D, Burnett RT, Goldberg MS, Hoover K, Siemiatycki J, Abrahamowicz M, White WH, et al. (2000). "Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. A Special Report of the Institute's Particle Epidemiology Reanalysis Project." Health Effects Institute.

Krewski D; Jerrett M; Burnett RT; Ma R; Hughes E; Shi Y; Turner MC; Pope AC III; Thurston G; Calle EE; Thun MJ. (2009).Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality. Health Effects Institute. Cambridge, MA. Report Nr. 140.

Laden F, Schwartz J, Speizer FE, Dockery DW. (2006). "Reduction in Fine Particulate Air Pollution and Mortality." Am J Respir Crit Care Med, 173:667-672.

Li N, Harkema JR, Lewandowski RP, Wang M, Bramble LA, Gookin GR, Ning Z, Kleinman MT, Sioutas C, Nel AE. (2010) Ambient ultrafine particles provide a strong adjuvant effect in the secondary immune response: implication for traffic-related asthma flares. Am J Physiol Lung Cell Mol Physiol. 299(3):L374-83.

McConnell R, Berhane K, Gilliland F, London SJ, Islam T, Gauderman WJ, Avol E, Margolis HG, Peters JM. (2002). "Asthma in exercising children exposed to ozone: a cohort study." Lancet, 359:386-91.

McConnell R, Berhane K, Gilliland F, London SJ, Vora H, Avol E, Gauderman WJ, Margolis HG, Lurmann F, Thomas DC, Peters JM. (1999). "Air Pollution and Bronchitic Symptoms in Southern California Children with Asthma." EHP, 107(9):757-760.

McConnell R, Berhane K, Gilliland F, Molitor J, Thomas D, Lurmann F, Avol E, Gauderman WJ, Peters JM. (2003). "Prospective Study of Air Pollution and Bronchitic Symptoms in Children with Asthma." Am J Respir Crit Care Med, 168:790-797.

National Research Council. (1998). "Research Priorities for Airborne Particulate Matter I: Immediate Priorities and a Long Range Research Portfolio." Washington, DC, National Academy Press.

Oberdorster G, et al. (1995). "Association of Particulate Air Pollution and Acute Mortality: Involvement of Ultra-Fine Particles." Inhalation Toxicol 7:111-124.

Peters J, et al. (1997). "Children's Health Study." http://www.arb.ca.gov/research/chs/chs.htm.

Pope III CA, Burnett RT, Thun MJ, Calle E, Krewski D, Kazuhiko I, Thurston G. (2002). "Lung Cancer, Cardiopulmonary Mortality, and Long-Term Exposure to Fine Particulate Air Pollution." JAMA, 287:1132-1141.

Pope III CA, Dockery DW. (2006). "Health Effects of Fine Particulate Air Pollution: Lines that Connect." JAWMA, Critical Review. 56(6):709-742.

Ritz B, Wilhelm M, Zhao, Y. (2006). "Air Pollution and Infant Death in Southern California, 1989-2000." Pediatrics. 118(2):493-502.

Ritz B, Yu F, Chapa G, Fruin S. (2000). "Effect of Air Pollution on Preterm Birth Among Children Born in Southern California between 1989 and 1993." Epidemiology, 11(5)502-11.

Ritz B, Yu F, Fruin S. Chapa G, Shaw GM, Harris JA. (2002). "Ambient Air Pollution and Risk of Birth Defects in Southern California." Am J Epidemiol, 155(1):17-25.

Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. (2000a). "Fine Particulate Air Pollution and Mortality in 20 U.S. Cities, 1987–1994." N Engl J Med, 343(24):1742-9.

Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, Schwartz J, Zanobetti A. (2000b). "The National Morbidity, Mortality, and Air Pollution Study Part II: Morbidity and Mortality from Air Pollution in the United States." Res Rep Health Eff Inst, 94-II.

SCAQMD. (2000). Multiple Air Toxics Exposure Study in the South Coast Air Basin. MATES II. South Coast Air Quality Management District. http://www.aqmd.gov/matesiidf/matestoc.htm

SCAQMD. (2008). Multiple Air Toxics Exposure Study in the South Coast Air Basin. MATES III. South Coast Air Quality Management District http://www.aqmd.gov/prdas/matesIII/matesIII.html.

Seaton A, et al. (1995). "Particulate Air Pollution and Acute Health Effects." Lancet 345:176-178.

Smith, RL; Xu, B; Switzer, P. (2009). Reassessing the relationship between ozone and short-term mortality in U.S. urban communities. Inhal Toxicol 21: 37-61.

U.S. EPA. (2000) Air Quality Criteria for Carbon Monoxide Final Report. U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment, Washington Office, Washington, DC, EPA 600/P-99/001F,

U.S. EPA. (2004) Air Quality Criteria for Particulate Matter (Final Report, Oct 2004). U.S. Environmental Protection Agency, Washington, DC, EPA 600/P-99/002aF-bF.

U.S. EPA. (2006a) Air Quality Criteria for Ozone and Related Photochemical Oxidants (2006 Final). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-05/004aF-cF.

U.S. EPA. (2006b) Air Quality Criteria for Lead. Final Report. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R

U.S. EPA. (2007a) Review of the National Ambient Air Quality Standards for Ozone: Policy Assessment of Scientific and Technical Information. OAQPS Staff Paper, EPA-452/R-07-007, July 2007.

U.S. EPA (2007b) Review of the National Ambient Air Quality Standards for Lead: Policy Assessment of Scientific and Technical Information OAQPS Staff Paper. EPA-452/R-07-013

U.S. EPA. (2008a) Integrated Science Assessment for Oxides of Nitrogen – Health Criteria (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/071.

U.S. EPA. (2008b) Integrated Science Assessment (ISA) for Sulfur Oxides – Health Criteria (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/047F.

U.S. EPA. (2009) Integrated Science Assessment for Particulate Matter (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-08/139F.

U.S. EPA. (2010). Integrated Science Assessment for Carbon Monoxide (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-09/019F.

U.S. EPA (2012) National Ambient Air Quality Standards for Particulate Matter. Proposed Rule. Federal Register,Vol. 77, No. 126, p.38890, Friday, June 29, 2012

U.S. EPA (2012b) Regulatory Impact Analysis related to the Proposed Revisions to the National Ambient Air Quality Standards for Particulate Matter EPA-452/R-12-003

Vedal S. (1997). Critical Review. Ambient Particles and Health: Lines that Divide. JAMA, 47(5):551-581.

Zeger S; Dominici F; McDermott A; Samet J. (2008). Mortality in the Medicare population and chronic exposure to fine particulate air pollution in urban centers (2000-2005). Environ Health Perspect, 116: 1614-1619.