State of California

Air Resources Board

Mary D. Nichols, Chairman

Governor Arnold Schwarzenegger

Public Comments on

Methodology for Estimating Premature Deaths Associated with Long-term Exposure to Fine Airborne Particulate Matter in California

Supplement to
Staff Report

October 24, 2008

California Environmental Protection Agency

Air Resources Board

California Environmental Protection Agency

Linda S. Adams, Secretary

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Introduction

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Alliance of Automobile Manufacturers- John Heuss (Air Improvement Resources), Sacramento, CA

American Enterprise Institute, Joel Swartz, Sacramento, CA

BNSF Railway, Topeka, KS

Diesel Technology Forum – Allen Schaffer, Frederick, MD

D. Warner North, NorthWorks, Inc., Belmont CA

Engine Manufacturers Association – Joseph L. Suchecki, Chicago IL

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John Dale Dunn, Carl R. Darnall Army Medical Center, Ft. Hood, TX

James Enstrom, UCLA, Los Angeles, CA

Union of Concerned Scientist/Environmental Defense Fund

Alliance of Automobile Manufacturers- John Heuss (Air Improvement Resources)

Comments on Air Resources Board May 22, 2008 Draft Staff Report "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California"

Prepared for the Alliance of Automobile Manufacturers

By

Jon M. Heuss

Air Improvement Resource, Inc.

July 11, 2008

Executive Summary

AIR, Inc. reviewed the draft report and finds a number of important concerns that severely limit its usefulness for estimating the health effects due to generic ambient $PM_{2.5}$ or diesel particulate matter. In particular, the pattern of results from the existing chronic and acute exposure studies is not consistent with the assumption inherent in the analysis that there is a mortality effect of generic ambient $PM_{2.5}$. The assumption inherent in regulating all $PM_{2.5}$ as if it were equally toxic is a gross simplification that is not consistent with the large body of toxicological data on either individual $PM_{2.5}$ components or ambient $PM_{2.5}$ mixtures. In addition, if low doses of generic ambient particles were causing the serious health effects implied by the statistical associations relied upon in the staff's analysis, then low doses of particles should be causing similar effects in other exposure situations. As shown in the body of these comments, this is not the case.

The draft report needs to consider the full range of results from chronic studies not just the positive studies and fully acknowledge the limitations to the use of the expert solicitation

The draft report relies heavily on the expert solicitation that was included in EPA's Regulatory Impact Analysis for the final 2006 PM rule. However, the expert solicitation did not address the key assumption that all fine particles, regardless of their chemical composition, are equally potent in causing premature mortality. This assumption leads to significant uncertainty in the state of knowledge about the health benefits associated with various emission reduction strategies.

Even though the draft report and the U. S. EPA acknowledges that the low end of the

credible range for mortality association from the expert solicitation is 0 %, the draft recommends a credible range from 3 % to 20 % per 10 µg/m^3 increase in $PM_{2.5}$. This arises because the draft omits consideration of negative chronic mortality studies, even though some of these studies were conducted in California.

The overall pattern of the epidemiological associations in the chronic studies as well as in acute studies is not consistent with a generic ambient $PM_{2.5}$ mortality signal

Rather than focus on the positive studies, CARB should evaluate the pattern in the full range of the literature. As documented in the body of these comments:

- There is a not a consistent mortality signal, when all the available studies are considered. There is a wide range of associations reported for both chronic and acute mortality with ambient $PM_{2.5}$. Although multi-city studies avoid publication bias, they also report a biologically impossible wide range of associations from positive to negative.

- There are a variety of opinions in the scientific community as to whether the fine PM associations in the literature are causal or not. The EPA's Criteria Document conclusion regarding causality is highly qualified and not consistent with the assumptions in the draft report's recommended methodology. It refers to as a growing body of evidence supporting the conclusion that "PM2.5 (or one or more PM2.5 components), acting alone and/or in combination with gaseous co-pollutants, are likely causally related to observed ambient fine particle-associated health effects."

- In order to apply the CARB methodology, the assumption of equal toxicity must be made. However, the assumption inherent in the current practice of measuring and regulating all $PM_{2.5}$ as if it were equally toxic is a gross simplification that is not consistent with the large body of toxicological data on either individual $PM_{2.5}$ components or ambient $PM_{2.5}$ mixtures. In addition, the patterns in the observational studies are not consistent with an effect of generic $PM_{2.5}$.

- Neither the pattern in observational studies nor the findings in controlled exposure studies is consistent with the CARB assumption that diesel $PM_{2.5}$ is equally toxic as generic $PM_{2.5}$. The lack of coherence between the large body of diesel health studies and the health signal in the studies the draft relies on should be acknowledged in the report.

There is much greater uncertainty than the draft acknowledges

The CARB report drastically understates the uncertainties inherent in applying the

proposed methodology. The report should acknowledge and discuss the following sources of uncertainty:

- The extent to which the effects reported in the long-term exposure studies are associated with historically higher levels of PM rather than the levels occurring during the study period is not known

- The extent to which adverse effects are associated with low-level exposures that occur many times in the year versus peak exposures is not known

- The fact that the differential toxicity of specific component species within the complex mixture of PM has not been determined

- The fact that that there are still major uncertainties in the interpretation of the long-term studies related to confounding by other pollutants, life-style factors, and the inappropriateness of the main analytical tool used in these studies.

- The fact that causality has not been established

- The fact that biological mechanisms have not been specifically identified for the presumed effect

- The fact that the strength of the presumed mortality effect from generic $PM_{2.5.}$ assumed in the draft is not consistent with a large body of information on the health effects of particles in other exposure situations

- The fact that, despite whatever opinions various experts might hold, the shape of the concentration-response function is not known

- EPA's Clean Air Scientific Advisory Committee (CASAC) strongly asserted its concern that the available epidemiological database does not establish either the presence or absence of threshold concentrations for adverse health effects

- For the federal risk assessment, the CASAC Panel favored the primary use of an assumed threshold of 10 $\mu g/m^3$ for both acute and chronic studies along with sensitivity analyses using other threshold assumptions

- Because of a lack of knowledge of the concentration-response function, EPA's risk assessment presented the results for a wide range of possible cut-off points from background up to 12 or 15 $\mu g/m^3$

- Because the shape is not known, ARB should evaluate cut-offs over the same range as EPA and because of all the uncertainties noted above, should include 0 % as the low end of the credible range

Finally, the report should acknowledge that, to the extent that the associations they are

utilizing are not caused by generic ambient $PM_{2.5}$, the benefits that the State expects will not occur.

The methodology for estimating ambient concentrations of $PM_{2.5}$ from diesel-fueled engines has severe limitations and should undergo a separate technical review

NOx is not a unique tracer for diesel emissions, in general, or for diesel $PM_{2.5}$. The ratio of DPM/NOx may be similar in many locations across California currently because the current mix of sources is similar. However, as various sources are controlled to a lesser or greater degree over time or as the mix of gasoline and diesel engines in use changes in time or space, the DPM/NOx ratio will change.

The new methodology is not needed for and is not relevant to the control of diesel emissions

Diesel emissions are already undergoing dramatic reduction throughout California based on a myriad of federal, state, and local control initiatives. The draft methodology is not needed to assure that the progress continues. Since diesel exhaust composition is changing dramatically, use of the draft methodology will needlessly alarm the public and may make the efficient use of newer, clean diesels more difficult. This could result in a less efficient transportation system and increased levels of greenhouse gas emissions.

Introduction

The methodology that California Air Resources Board (CARB) staff uses for quantifying health impacts from particulate matter (PM) exposure is similar to the methodology developed by the U.S. Environmental Protection Agency (EPA) for their regulatory impact analyses. The May 22, 2008 draft staff report[1] presents the results of a recent literature review related to the mortality effects of exposure to fine PM ($PM_{2.5}$) and recommendations for revisions to the current methodology.

In recent years, both EPA and CARB have used the $PM_{2.5}$/mortality associations from the American Cancer Society (ACS) study (Pope et al. 1995, 2002)[2] to estimate premature deaths associated with chronic $PM_{2.5}$ exposures. Several recent studies prompted CARB to update the $PM_{2.5}$ mortality relationship. In particular, the draft report notes the Jerrett et al. (2005) analysis of data in the Los Angeles region, the Laden et al. (2006) follow-up to the Harvard Six Cities study, the intervention study by Clancy et al. (2002) examining the effect of significant decreases in air pollution in Dublin, and clinical and toxicological studies (Sun et al. 2005) that suggest mechanisms by which

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[1.] California Air Resources Board, May 22, 2008 Draft Staff Report "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California"

[2.] References denoted by author and year in this report without a footnote are references in the CARB draft.

PM exposure may contribute to the cardiovascular disease process. In addition, the draft report relies heavily on a study carried out for EPA in which the opinions of twelve experts on the $PM_{2.5}$-mortality relationship were elicited and analyzed.

The new relative risk factor developed in the draft report is a 10% increase in premature death per 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration (with an uncertainty interval of 3% to 20%). Previously, CARB used a 6 % increase per 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration. Also, staff proposes to use a range of thresholds or cut-off levels between 2.5 and 7 $\mu g/m^3$. Using this approach, staff concludes that recent exposures to ambient $PM_{2.5}$ in California can be associated with about 14,000 to 24,000 premature deaths statewide annually, with uncertainty ranging from 4,300 to 41,000 deaths. Using this new methodology and assuming that diesel PM is as equally toxic as $PM_{2.5}$, staff estimated diesel PM contributes to 3,900 (uncertainty interval 1,200 to 7,100) premature deaths, statewide on an annual basis.

The draft report also indicates that the methodologies and results are endorsed by several of ARB's scientific advisors - Dr. Jonathan Levy of Harvard University, Dr. Bart Ostro of the Office of Environmental Health Hazard Assessment, and Dr. Arden Pope of Brigham Young University. In addition, the report underwent an external peer review by experts selected with the assistance of the University of California at Berkeley, Institute of the Environment.

AIR, Inc. reviewed the draft report and finds a number of important concerns that severely limit its usefulness for estimating the health effects due to generic ambient $PM_{2.5}$. In particular, the pattern of results from the existing chronic and acute exposure studies is not consistent with the assumption inherent in the analysis that there is a mortality effect of generic ambient $PM_{2.5}$. The assumption inherent in the current practice of measuring and regulating all $PM_{2.5}$ as if it were equally toxic is a gross simplification that is not consistent with the large body of toxicological data on either individual $PM_{2.5}$ components or ambient $PM_{2.5}$ mixtures. Because of such concerns, the U. S. EPA Administrator chose not to rely on the quantitative risk assessment in making the recent revisions to the National Ambient Air Quality Standards for $PM_{2.5}$. Instead, he evaluated the weight of evidence from the available observational studies considering both their strengths and limitations. Finally, if low doses of generic ambient particles were causing the serious health effects implied by the statistical associations relied upon in the staff's analysis, then low doses of particles should be causing similar effects in other exposure situations. As shown below, this is not the case. In the following sections, detailed comments are provided on the draft report documenting these and several additional concerns.

Comments on CARB summary of health studies on long-term PM exposures and premature death

The draft report includes summaries of the main long-term PM exposure studies. Much of the discussion as well as Table 1 was adapted with the authors' permission from the 2006 Critical Review in the Journal of Air and Waste Management Association by Pope and Dockery.[3] Pope and Dockery indicated that their 2006 review was not intended to be a point-by-point discussion of the issues that were presented in the 1997 Critical Review by Vedal.[4] Rather they indicated that their objective was to review the lines of research since 1997 that help connect the dots concerning the health effects of fine particulate focusing primarily on epidemiologic or human studies. Discussants of the review were disappointed that the authors chose this more limited objective since, as they acknowledge, there is substantial controversy over the interpretation of the epidemiological associations related to PM health effects.[5] Too often the scientists that accept certain associations as causal and those that are skeptical are talking past one another rather than to one another. Unfortunately, Pope and Dockery did not present the evidence both for and against various hypotheses and then weigh and discuss that evidence. The CARB draft report is subject to the same criticism.

Pope and Dockery acknowledge the presence of both positive and negative studies reporting associations of long-term exposure to fine PM and mortality. In 1997, EPA relied heavily on two cohort studies, the Six-City study[6] and the ACS study[7] that reported associations of fine PM and sulfate with cardiopulmonary deaths. In a careful re-analysis of these two studies a Health Effects Institute (HEI)-sponsored team[8] replicated the results that show an increased risk in the range of 7 to 14 % for all-cause mortality and 12 to 19 % for cardiopulmonary mortality associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$. However, the re-analysis also showed that 1) the increased risk was cardiovascular not respiratory, 2) one gaseous pollutant, SO_2, had a strong association with mortality, 3) when SO_2 was included in the model the PM all-cause mortality association was materially reduced and became non-significant, 4) the increased mortality was experienced in the portion of the cohort that had a high school education or less, and 5) there was a significant spatial heterogeneity in the association, with no effect seen in western U. S. cities.[9] All these additional findings raise questions

[3] Pope, C.A. III; Dockery, D. W. Health Effects of Fine Particulate Air Pollution: Lines that Connect; J. Air & Waste Management Assoc. 2006, 56, 709-742.
[4] Vedal, S. Critical Review-Ambient Particles and Health: Lines that Divide; J. Air & Waste Management Assoc. 1997, 47, 551-581.
[5] Heuss, J. and Wolff, G. J. Air & Waste Management Assoc. 2006, 56, 1368-1380.
[6] Dockery, D.; Pope, C.; Xu, X.;Spengler, J.; Ware, J.; Fay, M.; Ferris, B.; Speizer, F.; An association between air pollution and mortality in six U. S. cities, N. Engl. J. Med., 1993, 329, 1753-1759.
[7] Pope, C. A.; Thun, M. J.; Namboodiri, M. N.; Dockery, D. W.; Evans, J. S.; Speizer, F. E.; Heath, C. W.; Particulate air pollution as a predictor of mortality in a prospective study of U. S. adults, Am. J. Resp. Crit. Care Med., 1995, 151, 669-674.
[8] Krewski, D.; Burnett, R. T.; Goldberg, M. S.; Hoover, K.; Siemiatycki, J.; Jerrett, M.; Abrahamowicz, M.; White, W.; Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality, Health Effects Institute Special Report, 2001.
[9] Grant, L.; EPA Staff Presentation to CASAC, July 23, 2001; Key Revisions and Scientific Issues for Second External Review Draft of Air Quality Criteria for Particulate Matter; Slide 46 indicates an excess risk from 10 $\mu g/m^3$ $PM_{2.5}$ in the ACS cohort of +29 % in the Industrial Midwest, +25 % in the Southeast,

concerning the interpretation of the $PM_{2.5}$ associations as a universally applicable chronic PM health effect caused by generic $PM_{2.5}$.

The ACS study was updated by Pope et al. 2002[10] following the cohort for a total of 16 years. The PM and SO_2 associations persisted and the education effect persisted, but the authors did not evaluate the east/west difference or the impact of including both PM and SO_2 in the model. This is a serious omission. The Laden et al. (2006)[11] study extended follow-up of the Six Cities cohort by eight years to 1998. In the original Six City Study the mortality rates were plotted against various pollution measures and $PM_{2.5}$ gave the best fit. However, in the update, only $PM_{2.5}$ was evaluated and the fit in the second period is very poor. The poor fit in the second period is masked in their Figure 2b by plotting the results for both time periods in the same figure. Because of the poor fit with $PM_{2.5}$ in the update, other pollutants should be evaluated in this data set.

In both these updates, the authors neglected to carry out the same analyses that had been conducted in the original study. This is a serious oversight and is an example of the subtle way that confirmation bias creeps into the literature.

As Pope and Dockery and the draft CARB report indicate, there are other cohort studies of interest. A Veteran's Administration (VA) cohort[12] of 70,000 has been followed for 26 years with mixed results as noted by Pope and Dockery and CARB. In the latest report from this cohort, it is shown that previously unconsidered spatial covariates such as traffic or population density are strong predictors of mortality. The CARB report notes that the VA studies are not robust to model selection and other analytic decisions.

In California, a cohort of 6,338 non-smoking Seventh Day Adventists[13] has been followed for 22 years. As noted in Table 1, no significant positive associations of PM with mortality were found with 15 years of follow-up (the excess cardiopulmonary risk for 20 $\mu g/m^3$ PM_{10} was 0.6 % with 95th percentile confidence limits of -8%, 10%). Although the Chen et al. (2005)[14] update reports a positive association with a subset of cardiovascular deaths in females but not males, they include a comment that in

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+14 % in the Northeast, and –9 % in the West (West is a combination of cities in the Northwest, Southwest, Upper Midwest, and Southern California. NMMAPS geographic regions).

[10] Pope, C. A.; Burnett, R.; Thun, M.; Calle, E.; Krewski, D.; Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution," J. American Medical Assoc., 2002, 287, 1132-1141.

[11] Laden, F.; Schwartz, J.; Speizer, F.; Dockery, D.; Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-Up of the Harvard Six-Cities Study; Am. J. Respir. Crit. Care Med., 2006, 173,667-672.

[12] Lipfert, F.;Perry, H.; Miller, J.; Baty, J; Wyzga, R.; Carmody, S.; The Washington University-EPRI veterans' Cohort Mortality Study: Preliminary Results, Inhalation Toxicol., 2000, 12 (suppl. 4), 41-73.

[13] Abbey, D. E.; Nishino, N.; McDonnell, W. F.; Burchette, R. J.; Knusten, S.F.; Beeson, W. L.; Yang, J. S,; Long-Term Inhalable Particles and Other Air Pollutants Related to Mortality in Non-Smokers, Am. J. Resp. Crit. Care Med., 1999, 59, 373-382.

[14] Chen, L.H.; Knutsen, S.F.; Shavlik, D.; Beeson, W.L.; Petersen, F,; Ghamsary, M.; Abbey, D.; The Association between Fatal Coronary Heart Disease and Ambient Particulate Air pollution: Are Females at Greater Risk?; Environ. Health Perspect., 2005, 113, 1723-1729.

extended follow-up of cardiopulmonary mortality in the total AHSMOG cohort through 1998 using the same models as previously, "we continue to find slightly stronger association in males than in females (unpublished data)." The fact that Chen et al. do not report these results suggests that their update found no overall cardiopulmonary effect, so this study does not support the ACS and Six-City findings. The omission of results calculated in a way that can be directly compared with the earlier study and with other studies in the literature is a serious oversight. Since this is a California study, CARB should contact the authors and request the data be provided on a basis that can be compared to the other studies in the literature.

The Enstom (2005)[15] study of a cohort of 36,000 in 11 California counties is also negative as noted by Pope and Dockery. As noted during the June 25, 2008 workshop, this is also an important study for CARB to consider in the review.

The CARB draft relies heavily on the Jerrett et al. 2005 study that reported higher fine PM/premature death associations in the 23,000 members of the ACS cohort that lived in metropolitan Los Angeles. However, there is additional information in an extended follow-up and spatial analysis of the ACS cohort being carried out for the Health Effects Institute that found that, unlike the Los Angeles results, "mortality for all-cause, cardiopulmonary, and lung cancer deaths was not elevated in the New York spatial analysis."[16] The new HEI study reports, in agreement with earlier analyses, that the $PM_{2.5}$ signal in the ACS cohort is an association with had shown that the $PM_{2.5}$ signal in this cohort is cardiovascular and not respiratory; in fact, elevated $PM_{2.5}$ appeared to be somewhat protective against respiratory deaths.

Jerrett et al. 2005 extracted data on almost 23,000 subjects in the Los Angeles area from the ACS cohort for the period 1982–2000, with more than 5,000 deaths. Pollution exposures were interpolated from 23 fine PM and 42 ozone fixed-site monitors. After controlling for 44 individual covariates, they reported a significantly increased risk of mortality associated with fine PM for all-cause, ischemic heart disease, and lung cancer mortality. The only joint pollutant analyses were with ozone, and the authors conclude that the PM results were robust to adjustments for ozone and expressway exposure. The authors also state that the magnitude of fine PM effects are about three times as large as those found in earlier studies, the clear implication being that the better exposure estimates obtained by interpolation of the pollution data "suggest the chronic health effects associated with within-city gradients in exposure to $PM_{2.5}$ may be even larger than previously reported across metropolitan areas." However, when contextual covariates related to socioeconomic status were included in the analyses, the associations of fine PM with total, ischemic heart disease, and lung cancer mortality were substantially attenuated and became either insignificant or only borderline significant.

Moreover, although SO_2 was strongly associated with mortality in the Krewski

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[28] Enstrom, J.E.; Particulate Air Pollution and Total Mortality Among Elderly Californians, 1973-2002; Inhal. Toxicol., 2005, 17, 803-816.

[16] Krewski, D. et al. ; Health Effects Institute Annual Conference 2008, Program and Abstracts, abstract at page 33.

reanalyses, surprisingly Jerrett et al. considered no co-pollutants other than ozone. In time-series analyses in Los Angeles various gases including CO and SO_2 have been found to be associated with mortality even though concentrations of SO_2 are low. Particularly in view of the strong association reported for ischemic heart disease in this study, CO should have been considered as a potential confounder. Finally, the RR for lung cancer in this study (1.44 without the contextual covariates) is much higher than that reported in any of the previous analyses of the ACS II cohort which is much too high to be biologically plausible. Unfortunately, the paper does not present the relative risks associated with strong risk factors, such as cigarette smoking, estimated in this study. In epidemiologic studies, the estimated risks from such factors are often used as a 'reality check' of whether the analyses yield reasonable estimates of well-studied risk factors.

The CARB draft also discusses the Netherlands pilot study, Hoek et al. 2002, and indicates that a more recent study of the same cohort, Beelen et al. 2008, reinforces the conclusions of the pilot study and lends convincing support to the link between premature death and PM. This description is misleading. First, the 2008 study involved the full cohort of over 120, 000 subjects whereas the pilot study was only 5,000 subjects from the cohort. Second, the associations in the full cohort were much lower than for the pilot study, with none of the $PM_{2.5}$ associations in the full cohort being statistically significant. Third, the strongest associations were with respiratory mortality. Thus, although Beelen et al. assessed air pollution on an even finer spatial scale than Jerrett et al., they report lower relative risks and a respiratory signal as compared to the cardiovascular signal in the ACS cohort. Finally, Beelen et al. conclude that their results add to the evidence that long-term exposure to ambient air pollution (rather than $PM_{2.5}$) is associated with increased mortality.

The draft also includes a discussion of the Women's Health Initiative Study that reported higher cardiovascular risk estimates than the other studies. However, scientists from Exponent, Inc.[17] have pointed out that the within-city risk (the risk associated with differences in fine PM levels within cities) for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ is greater than the risk associated with smoking 40 cigarettes a day, findings that defy plausibility, casting doubt on the results of the study.

After summarizing the individual studies, the CARB draft indicates that evaluating which studies to consider in assessing the public health impacts of air pollution is a difficult task. It goes on to introduce the EPA expert solicitation, describe the solicitation and its results, and then base the CARB recommended methodology, in large part, on the results of the solicitation. Since the expert solicitation plays such a large role in the draft report, the limitations of the solicitation need to be fully discussed in the draft.

Limitations of the EPA expert solicitation

The draft indicates that the elicitation was recommended by both the National Research Council (NRC 2002) and the Science Advisory Board (U.S EPA 2004). While true, it is

[17] J. Turim, S. Moogavkar, and E. Anderson, Comments on EPA's Integrated Science Assessment for Sulfur Oxides-Health Criteria, Exponent, Inc. Report, November 30, 2007.

important to remember the context in which expert solicitation is recommended. The NRC report recommended that EPA carry out a comprehensive probabilistic multiple-source uncertainty analysis for its health risk and impact assessments. Due to the lack of data on certain key issues, the NRC panel recommended expert solicitation to augment the data-driven uncertainty analysis. The NRC recommended that probability distributions for all major sources of uncertainty be developed. The NRC also recommended that EPA put the results of the analysis in context by referring not only to the absolute numbers of avoided adverse health outcomes but also to total projected numbers of these outcomes and to population sizes. Thus, an estimated number of avoided deaths in a given year should be accompanied by the total number of deaths and the population size in that year. The panel also recommended that EPA should strive to present the results in ways that avoid conveying an unwarranted degree of certainty such as presenting fewer significant digits and emphasizing ranges rather than single numbers.

When viewed in context with these recommendations, the EPA expert solicitation must be viewed as a useful first step in evaluating the use of expert advice but not as a sound basis for regulatory decisions. In fact, the description of the expert solicitation in the EPA's benefits analysis for the recent revisions to the $PM_{2.5}$ air quality standard and the Administrator's explanation of the rationale for his final decisions fully support the view that the expert solicitation does not address all the key uncertainties and, thus, is not a sound basis for regulatory decisions.

For example, Chapter 5 of the EPA's Regulatory Impact Analysis (RIA) for the final 2006 PM rule notes three key assumptions that underly the mortality concentration-response functions used in the RIA: that inhalation of fine particles is causally associated with premature death at concentrations near those experienced by most Americans on a daily basis, that all fine particles, regardless of their chemical composition, are equally potent in causing premature mortality, and that the C-R function for fine particles is approximately linear within the range of ambient concentrations under consideration above an assumed threshold of 10 $\mu g/m^3$. The RIA goes on to indicate that the expert solicitation addressed the first and third of these assumptions but did not directly address the second. This is a very important oversight. The assumption of equal toxicity makes the type of analysis in the EPA RIA and the CARB draft report simple and straightforward, but it is not scientifically sound. The EPA RIA acknowledges that the assumption of equal toxicity remains a significant source of uncertainty in the state of knowledge about the health benefits associated with various emission reduction strategies.

The Administrator, in the final PM rule, carefully considered the quantitative risk assessment, but concluded that because it is based on studies that do not resolve a number of key uncertainties (regarding the shape of concentration-response functions, the issue of a threshold, and the differential toxicity of various PM components) it does not provide an appropriate basis for selecting the levels of the short-term or long-term standard.[18]

[18] 71 FR 61168, October 17, 2006.

The CARB report needs to fully acknowledge the limitations of the quantitative use of the expert solicitation.

Comments on development of the methodology

In Section IIC and IID, the CARB report discusses the strengths and weaknesses of the various cohort studies and uses various screening criteria to arrive at the conclusion that the ACS and Six City studies should be used as the primary evidence for C-R functions. This discussion is biased in that it gives a series of reasons why the chosen studies are appropriate and a series of reasons why California studies such as Enstrom and AHSMOG should not be considered. Then in Section IID, various options for pooling the three chosen studies - Pope et al. (2002), Laden et al. (2006), and Jerrett et al. (2005) – are presented. The results are presented in Table 3. By relying only on these positive studies, a credible range of between 3 % and 20 % increase in mortality risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ is proposed. The results from pooling the expert solicitation data is also shown, with a range between 0 % and about 20 %. The ranges are similar because the experts indicated they placed most emphasis on the positive studies cited by CARB. However, the low end of the range was 0 %. The U. S. EPA PM RIA also acknowledges that the low end of the credible range for mortality association from the expert solicitation is also zero. If CARB staff had included the Enstrom and AHSMOG results, it is likely the low end of their credible range would have also been 0 %. Thus, by excluding relevant studies from their thinking, CARB has biased the results high.

The overall pattern of the epidemiological associations in the chronic studies as well as in acute studies is not consistent with a generic ambient $PM_{2.5}$ mortality signal

Rather than focus on the positive studies, CARB should evaluate the pattern in the full range of the literature. As the various chronic and acute exposure studies are considered, four questions come to mind. They are:

Are there consistent associations reported in these studies?

Are the associations causal?

Are the associations consistent with a mortality effect of generic $PM_{2.5}$?

Do the associations implicate diesel PM as equally toxic as generic PM?

Are there consistent associations reported in these studies?

There is a wide variation in the reported associations in the cohort studies listed in Table 1 of the CARB report. The wide variation holds for all-cause mortality as well as for separate causes of death, such as cardiovascular and respiratory. For example, Laden 2006 reports a strong cardiovascular signal in the Six City Study that results in a significant all-cause signal, but Enstom in 11 California counties reports no overall elevation of risk. In the large Dutch study (Beelen 2008) there is a weak respiratory signal, but in the large ACS cohort, Pope et al. 2004 report a strong cardiovascular signal along with a somewhat protective effect of fine PM on respiratory causes of death.

Although the CARB report does not discuss the acute mortality studies in detail, there is ample evidence of an implausibly wide range in individual city associations in numerous multi-city studies. For example, the Franklin et al. 2007 study of acute mortality in 27 U. S. cities noted in the CARB draft reports individual city associations ranging from – 5 % to + 10 % per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Franklin et al. discuss the cities with strong positive associations but never acknowledge the strong and statistically significant negative associations in cities like Houston and Dallas. They do note that there is stochastic variability in their results. There are now many multi-city studies that show the same implausibly wide range, both with $PM_{2.5}$ and with PM_{10}. Dominici et al.[19] acknowledge that the city-specific maximum likelihood estimates from their study of the 88 largest U. S. cities range from - 4 to + 4 % per 10 $\mu g/m^3$ increase in PM_{10}. This translates into a range of - 8 % to + 8 % (with a combined estimate of 0.4 %) for a 20 $\mu g/m^3$ PM_{10} increase, an increment that would roughly correspond to a 10 $\mu g/m^3$ increase in $PM_{2.5}$. In the Katsouyanni et al. (2003)[20] 29-city European multi-city study, the range in total mortality associations was also very wide, from – 1.6 % to + 2.7 % per 20 $\mu g/m^3$ increase in PM_{10}. In the Analitis et al. (2006)[21] report on respiratory and cardiovascular associations from the same cities, the range is also large for each category of death, with negative associations in some cities, but positive associations in the bulk of the cities. However, for six of the twenty-one cities in which there was a negative association for either respiratory or cardiovascular death, the association for the other cause of death was strongly positive, which is biologically implausible. For example, in Stockholm, the associations were + 16 % for cardiovascular death and – 1.7 % for respiratory death per 20 $\mu g/m^3$ increase in PM_{10}. The pros and cons of combining such disparate results and reporting a combined association need to be

[19] Dominici, F.; McDermott, A.; Zeger, S. L.; Samet, J. M.; National Maps of the Effects of Particulate Matter on Mortality: Exploring Geographic Variation, Environmental Health Perspectives, 2003, 111, 39-43.

[20] Katsouyanni, K.; Touloumi, G.; Samolu, E.; Petasakis, Y.; Analitis, A.; Le Tertre, A., Rossi, G.; Zmirou, D.; Ballester, F.; Booumghar, A.; Anderson, H. R.; Wojtyniak, B.; Paldy, A.; Braustein, R.; Pekkanen, J.; Schindler, C.; Schwartz, J.; Sensitivity Analysis of Various Models of Short-Term Effects of Ambient Particles on Total Mortality in 29 Cities in APHEA2. In: Revised Analyses of Time-Series Studies of Air Pollution and Health, Health Effects Institute, Boston, MA, p. 157-164, 2003

[21] Analitis, A.; Katsouyanni, K.; Dimakopoulou, K.; Samoli, E.; Nikoloulopoulos, A. K.; Petasakis, Y.; Touloumi, G.; Scwartz, J.; Anderson, H.R.; Cambra, K.; Forastiere, F.; Zmirou, D.; Vonk, J.M.; Clancy, L.; Kriz, B.; Bobvos, J.; Pekkanen, J.; Short-Term Effects of Ambient Particles on Cardiovascular and Respiratory Mortality, Epidemiol. 2006, 17, 230-233.

carefully considered by the scientific community. To date, the implausible wide range of results has been essentially ignored.

A multi-city study was conducted in nine heavily populated California counties by Ostro et al.[22] The combined association highlighted in the study, 0.6 % per 10 µg/m^3, is less than half the combined association reported in the original Schwartz et al. six-city study that EPA relied upon when setting the first $PM_{2.5}$ NAAQS in the 1996/97 review. However, the complete results Ostro et al. report suggest that the combined fine PM association is smaller and less robust than reported in their abstract and conclusions. Ostro et al. report analyses using natural splines as well as penalized splines to smooth for temporal trends, each with varying degrees of freedom. As the degrees of freedom increased, the association became smaller and less significant. None of the all-cause mortality associations were statistically significant using natural splines. The authors also report that most of the fine PM mortality associations were attenuated in multi-pollutant models with CO or NO_2 but no results are shown. Thus, in total, the combined fine PM association is weaker, less significant, and less robust than the authors infer when all the analyses carried out are considered.

The Ostro study is particularly important because the average $PM_{2.5}$ levels in the California counties they studied are among the highest in the U. S. ranging from 14 to 29 µg/m^3. There appears to be little relation between the nine individual effect estimates and the fine PM levels. The strongest and weakest associations occur in counties with nearly identical fine PM concentrations and the county with the highest concentrations, Riverside, has no evidence of a significant association. Interestingly, Los Angeles and Riverside had slightly negative $PM_{2.5}$ associations in the Franklin et al. 2007 study while Sacramento and San Diego had positive associations. In summary, the overall pattern in both acute and chronic studies in California and across the nation is not consistent.

An important HEI study[23] (that is not referenced in the Pope and Dockery review) is also relevant. The HEI study evaluated coherence between the time-series associations of mortality and hospital admissions in 14 cities. It found little or no coherence between the PM_{10} mortality and morbidity associations and, importantly, found little or no correlation between the time series of health event counts (mortality and hospital admissions) in the various cities. As in other multi-city studies, the individual associations for mortality and morbidity covered a wide range from positive to negative.

Publication bias is another factor to consider in evaluating this literature. Editors have little interest in publishing and authors have little interest in submitting “no effect” studies. We note that there is a strong tendency to report and highlight some positive

[22] Ostro, B.; Broadwin, R.; Green, S.; Feng, W.-Y.; Lipsett, M.; Fine Particulate Air Pollution and Mortality in Nine California Counties: Results from CALFINE; Environ. Health Perspect. 2006, 114, 29-33.
[23] Dominici, F.; Zanobetti, A.; Zeger, S. L.; Schwartz, J.; Samet, J.; The National Morbidity, Mortality and Air Pollution Study Part IV: Hierarchical Bivariate Time-Series Models-A Combined Analysis of PM_{10} Effects on Hospitalizations and Mortality, Health Effects Institute, HEI Research Report 94, Part IV, 2005.

result in all the chronic studies noted in Table 1 of the CARB report. In the AHSMOG update by Chen et al., a positive signal in women for a subset of cardiovascular mortality is highlighted but the overall cardiopulmonary associations are not reported. If they were significantly positive, they presumably would have been reported. In an earlier AHSMOG study, McDonnell et al. 2000, a positive association for males was stressed but the negative association for females was downplayed. In the French PAARC study, there was no statistically significant association with any pollutant, but a positive association was found when a subset of monitors was used.

In the acute studies, publication bias tends to be a major concern inflating the size of any true effect. Goodman[24] notes that depending on published single-estimate, single-site analyses is an invitation to bias. He notes that investigators tend to report, if not believe, the analysis that produces the strongest signal and that there are innumerable model choices that affect the estimated strength of that signal. Although multi-city studies avoid publication bias, as we show above, they also report a biologically impossible wide range of associations from positive to negative. Thus, there is a not a consistent mortality signal, when all the available studies are considered. There is a wide range of associations for both chronic and acute mortality with ambient $PM_{2.5}$.

Are the associations causal?

There are a variety of opinions in the scientific community as to whether the fine PM associations in the literature are causal or not. The extensive literature reviewed in EPA's Criteria Document (CD)[25] is referred to as a growing body of evidence supporting the conclusion that "PM2.5 (or one or more PM2.5 components), acting alone and/or in combination with gaseous co-pollutants, are likely causally related to observed ambient fine particle-associated health effects."

In regard to confounding by other environmental variables, the CD concludes that "much uncertainty remains" and that "no clear consensus yet exists as to what methods may be appropriate or adequate for specific cases." Nevertheless, the CD indicates that the evidence tends to substantiate that "observed PM effects are at least partly due to PM acting alone or in the presence of other co-varying gaseous pollutants."[26]

Regarding model selection, the CD indicates that the data appear to demonstrate PM risks beyond those attributable to weather influences alone, even though there is no clear consensus at this time as to what constitutes appropriate or adequate model specifications to control for possible weather contributions.

When these conclusions are considered together, it is clear that the case for PM health effects is still highly uncertain. The many qualifications put on these conclusions in the CD indicate that there are still major methodological issues and uncertainties regarding

[24] Goodman, S. N.; The Methodologic Ozone Effect, Epidemiology, 2005, 16, 430-435.
[25] U.S. EPA, Air Quality Criteria for Particulate Matter; EPA/600/P99/002aF and bF; U.S. Environmental Protection Agency, Washington, DC, 2004, at page 8-388.
[26] CD at page 8-340.

how the PM associations should be interpreted. Pope and Dockery, in their review, also note the need for continued healthy skepticism.

The experts that participated in EPA's solicitation had varying views as to their confidence that the associations were causal, with responses varying from 30 % to 99%. However, the experts were not asked their views on the assumption of equal toxicity of all PM components. Therefore, their responses should be taken as support for the view, consistent with EPA staff and CASAC, that $PM_{2.5}$ (or one or more $PM_{2.5}$ components) are likely causal in the positive cohort studies. Each expert provided both upper and lower bound estimates for the concentration-response function. In three cases, the lower bound estimate was that there was no premature mortality caused by $PM_{2.5}$. This is shown in Figure 5-16 of EPA's Regulatory Impact Analysis. Thus, the lower bound assumed by CARB should also be zero.

Are the associations consistent with a mortality effect of generic $PM_{2.5}$?

In order to apply the CARB methodology, the assumption of equal toxicity must be made. However, the assumption inherent in the current practice of measuring and regulating all $PM_{2.5}$ as if it were equally toxic is a gross simplification that is not consistent with the large body of toxicological data on either individual $PM_{2.5}$ components or ambient $PM_{2.5}$ mixtures. In addition, the patterns in the observational studies are not consistent with an effect of generic $PM_{2.5}$.

PM air pollution is a complex mixture of solid and liquid particles that vary in number, size, shape, surface area, chemical composition, solubility, and origin. The PM CD[27] indicates that different PM materials also vary extensively in toxicity based on over 30 years of toxicological study. The CD concludes that the historical toxicological data provide little basis for concluding that specific PM constituents have substantial respiratory effects at current ambient levels. This substantial body of information is routinely used to establish chemical-specific standards that are used in occupational and other settings and demonstrates that the relative toxicity of different $PM_{2.5}$ species per unit mass varies by over three orders of magnitude.[28]

In the high dose studies reviewed in Chapter 7 of the CD, there are many examples that show that biological response varies dramatically depending on the chemical composition of the PM used. The CD summarizes this material noting "overall, the new studies suggest that some particles are more toxic than others." The CASAC specifically commented on this issue indicating "The chapter must make it clear that there is a large data base that indicates that PM is markedly variable in its toxic potency." [29] Thus, the assumption that all PM is equally toxic cannot be supported and the current practice of measuring and regulating all $PM_{2.5}$ as if it were equally toxic is a gross simplification that leads to substantial uncertainty

[27] CD at page 7-85.
[28] 2006 Threshold Limit Values and Biological Exposure Indices, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio.
[29] Hopke, P.; Clean Air Scientific Advisory Committee (CASAC) Particulate Matter (PM) Review Panel's Ongoing Peer Review of the Agency's Fourth External Review Draft of Air Quality Criteria for Particulate Matter, EPA-SAB-CASAC-04-005, U.S. EPA, Washington, DC, March 1, 2004.

One of the methods used to study ambient PM in a semi-controlled way is to expose humans or animals to ambient air particles that have been concentrated by a factor of 6 to 12. In studies with concentrated ambient air particles (CAPS), no consistent pattern of inflammatory changes has emerged. Some of these studies are referred to in Table 7 of the Pope and Dockery review as having somewhat mixed results, but with small increases in neutrophils and fibrinogen consistent with mild inflammatory responses to PM. The few statistically significant changes that have been reported in these studies are small, transient, and within the normal physiologic range. It is not clear if these changes are small but real changes that are not consistent because of the varying composition of the PM or if they are changes within the normal range solely due to chance.

The synopsis[30] of a recent HEI report on CAPS, diesel exhaust exposures and inflammation notes that "a consistent pattern of inflammation after exposure to a variety of PM mixtures in many studies has not emerged to date." The synopsis notes for example that "many markers of inflammation were studied but few changed; of those that changed, the magnitude of the change was modest." It was also noted that "because so few markers of inflammation changed in the current studies, it is possible that these changes occurred by chance." Thus, with exposures to elevated concentrations of concentrated ambient particles there are, at the most, small transient changes that are within the normal physiologic range and not of clinical significance. Such changes are not likely able to explain the epidemiologic associations.

In another recent CAPS paper, Kodavanti et al.[31] report on a series of short-term exposures of two strains of rats, one of which was bred to be spontaneously hypertensive. Six one-day exposure studies of the two strains of rats exposed to $PM_{2.5}$ between 1138 and 1765 $\mu g/m^3$ found no biological effects compared to filtered air controls. Seven two-day exposure studies with $PM_{2.5}$ between 144 and 2758 $\mu g/m^3$ reported small changes in a number of biochemical markers. However, the authors concluded that no biological effects correlated with CAPS mass. Rather, the authors concluded that the biological effects appeared to depend on chemical composition. This study adds additional support to the conclusion from a great deal of toxicological data that it is PM composition not PM mass that determines any PM health effects.

The CARB draft and the expert solicitation relied heavily on the Sun et al. 2005 toxicological study that suggests a mechanism by which PM could contribute to cardiovascular disease. However, the acceleration of atherosclerosis in this highly susceptible mouse model is not specific to PM and is not likely caused by diesel PM. Mauderly has shown that the susceptible mouse model responds to some gases without the presence of PM. In addition, the initial results of the HEI's NPACT study, as reported by Lippmann at the recent HEI annual conference,[32] showed dramatically

[30] Holgate, S. T. et al.; Health Effects of Acute Exposure to Air Pollution, Health Effects Institute, Research Report 112, December 2003.
[31] Kodavanti, U. P.; Schladweiler, M. C.; Ledbetter, A. D.; McKee, J. K.; Walsh, L.; Gilmour, P. S.; Highfill, J. W.; Davies, D.; Pinkerton, K. E.; Richards, J. H.; Crissman, K.; Andrews, D.; Costa, D. L.; Health Perspectives, 2005, 113, 1561-1568.
[32] Lippmann, M et al. "Characteristics of PM associated with health effects," poster at the Health Effects

different responses from CAPS exposures in Tuxedo, NY (where the Sun et al. 2005 work was conducted) and CAPS exposures in Manhattan. Lippmann reported that there were significant changes in atherosclerosis after 3 months in Tuxedo but not in Manhattan. The elemental carbon concentrations were three times higher in Manhattan than in Tuxedo, so whatever is causing the biological responses in the susceptible mouse model, it is not generic $PM_{2.5}$ and it is not diesel PM. The experts did not have the benefit of these further toxicological results so their opinions regarding PM causality are probably overly optimistic.

The overall patterns in observational studies are also not consistent with a generic $PM_{2.5}$ effect. As noted above, the health effects signal in the long-term cohort studies is a cardiovascular signal in the central and eastern portion of the U. S., with actually a negative association in the west. There are similar regional differences in the acute studies. Of the available multi-city studies, NMMAPS is the most comprehensive for mortality and the recent Dominici et. al. (2006) analysis is the most comprehensive for hospital admissions. Although NMMAPS used PM_{10} data, the PM signal would include both fine and coarse PM effects and the results have been evaluated by region. A seasonal NMMAPS analysis is now available.[33] Using updated mortality data from 1987-2000 in 100 cities, the analyses by season show that the combined association at lag 1 was greatest during the summer. Summer was the only season for which the combined effect was statistically significant. An analysis by geographical regions showed a strong seasonal pattern in the Northeast with a peak in the summer and little seasonal variation in the southern regions of the country. The authors acknowledge that there are several possible explanations for their results. One obvious hypothesis is that the most toxic particles have a spring/summer maximum and are more prevalent in the Northeast. Another mentioned by the authors is that there is a seasonally varying bias from an, as yet, unidentified source.

The Dominici et al.2006[34] study evaluated fine PM hospital admissions associations for 204 U. S. urban counties with a population greater than 200,000 using 1999-2002 Medicare hospital admission data. The results are presented for a two stage Bayesian analysis for various types of admissions and by region. Combined associations of the order of 1 % increase in various cardiovascular or respiratory outcomes per 10µg/m^3 increase in $PM_{2.5}$ are reported. While this is a comprehensive and important analysis, there are several issues that render its interpretation as an effect of generic fine PM questionable. First, the authors present results from seven separate regions as well as a comparison of the three western regions with the four eastern regions. There is a clear difference in the combined associations among the regions and particularly between the eastern and western region. The combined association is positive for cardiovascular outcomes in the east but negative in the west except for heart failure that is positive in both areas. This is not consistent with an effect of generic $PM_{2.5}$ on cardiovascular hospital admissions and, indeed, the authors point out the need to shift

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Institute Annual Conference, April 27-29, 2008, Philadelphia, PA.

[33] Peng, R. D.; Dominici, F.; Pastor-Barriuso, R.; Zeger, S. L.; Samet, J. M.; Seasonal analyses of air pollution and mortality in 100 U. S. Cities, Am. J. Epidemiol., 2005, 161, 585-594.

[34] Dominici F.; Peng, D; Bell,; M.; Pham.; McDermott, A.; Zeger, S. L.; Samet, J. M.; Particles, Air Pollution and Hospital Admissions for Cardiovascular and Respiratory Diseases, J. American Medical Association, 2006, 295, 1127-1134.

the focus of research to identifying those characteristics of particles that determine their toxicity. The authors report strong evidence of spatial heterogeneity in the $PM_{2.5}$ associations.

Second, the authors present the results for a range of lags and then focus on the lag that provides the strongest combined association for each endpoint. This may bias the results. Until there is more data on the actual mechanisms of PM toxicity, it is uncertain if their choice of lags is consistent with the toxic action of PM or its components. Third, the authors acknowledge that the complex statistical models used may not eliminate all bias.

Although this is an important study, it is deficient in two major ways. First, the authors do not show any of the results of the first stage analysis. Based on other multi-city analyses by the same authors or other multi-city studies where the first stage results are presented, one would expect large variations in individual county associations in each region. For example, the 14 individual city NMMAPS estimates for cardiovascular admissions (Schwartz et al. 2003)[35] range from – 2 % to + 4.6 % per 20 $\mu g/m^3$ increase in PM_{10}, which is a biologically implausible range.

Thus, even though there may be an overall combined positive association in a given region with a given category of admissions, there are undoubtedly counties with both strong positive and strong negative associations in that region. This is an important finding that the authors do not disclose. It is important because it raises a serious concern over the issue of publication bias in the general literature. The authors argue that their approach of analyzing national data uniformly avoids the potential for publication bias when positive findings are selectively reported. Thus, the authors recognize the presence of potential publication bias. By showing all their first stage results and comparing the range of results with that in the general literature, the extent of publication bias for hospital admissions could be estimated. The authors do note that their combined result is several-fold lower than other associations they cite from the literature.

The second major deficiency has to do with consideration of other air pollutants. The authors only considered one other pollutant, ozone, and considered it only as a potential effect modifier. However, there is an ample literature of small positive associations of hospital admissions in single pollutant models with a range of air pollutants, particularly for heart failure, the admission for which they report the most consistent association.

Because there are significant regional differences in both acute and chronic observational studies, the assumption of equal toxicity cannot be supported. Therefore, this major source of uncertainty should be highlighted in the CARB report.

Do the associations implicate diesel PM as equally toxic as generic PM?

[35] Schwartz, J; Zanobetti, A.; Bateson, T.; Morbidity and Mortality among Elderly Residents of Cities with Daily PM Measurements, In: Revised Analyses of Time-Series Studies of Air Pollution and Health, Health Effects Institute, Boston, MA, p. 25-53, 2003.

The CARB report indicates that staff assumed diesel PM is equally toxic as $PM_{2.5}$. However, there is little evidence to support the notion that either generic $PM_{2.5}$ or diesel PM is responsible for the positive signals in the acute or chronic observational studies.

As noted above, the pattern of results for atherosclerotic susceptible mice between Tuxedo NY and Manhattan, with an effect in the low diesel exposure case and no effect in the high diesel exposure case, is not consistent with diesel PM causing the adverse health signal. In addition, the pattern of spatially resolved mortality effects between Los Angeles, New York and the Netherlands is not consistent with diesel PM causing the adverse health signal.

The adverse health signal in the ACS and Six City studies that the CARB methodology relies on is a cardiovascular signal. In contrast, the concern over health effects from diesel exhaust has concentrated on respiratory effects. There are numerous studies of diesel emissions and exposures that have been reviewed in comprehensive reports by the U. S EPA,[36] the Health Effects Institute[37] and by Hesterberg et al.[38] The EPA Health Assessment Document for Diesel Exhaust reviews the extensive animal and human studies of the effects of diesel and discusses numerous respiratory effects that may occur due to diesel exposure. However, in discussing the human studies that are primarily of occupational exposures, EPA concludes that "the absence of reported noncancerous human health effects, other than infrequently occurring effects related to respiratory symptoms and pulmonary function changes, is notable."[39] Regarding cardiovascular disease, EPA cites the Edling et al. 1987 study of a cohort of male bus garage employees followed from 1951 through 1983 in which no increased mortality from cardiovascular disease was found when compared with the general population or grouped as subcohorts with different levels of exposure. The lack of cardiovascular risk in occupational cohorts exposed to historic high concentrations of diesel is not coherent with diesel causing cardiovascular mortality at current ambient concentrations.

Based on the available information on non-cancer effects, the EPA developed a reference concentration, RfC, of 5 $\mu g/m^3$ as a chronic exposure likely to be without appreciable risk of adverse human health effects. To develop the RfC, EPA used the entirety of the data from many chronic studies from several different species and evaluated a myriad of possible diesel-specific toxicological endpoints. Given the many safety factors included in the development of the RfC, EPA also indicated that the 5

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[36] USEPA (2002). Health Assessment Document for Diesel Engine Exhaust. EPA/600/8-90/057F. Washington, DC, U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment.

[37] HEI (1995). Diesel exhaust: A critical analysis of emissions, exposure, and health effects. A special report of the Diesel Working Group of the Health Effects Institute. Boston, MA, Health Effects Institute; HEI (1999). Diesel emissions and lung cancer: Epidemiology and quantitative risk assessment. Special report. Boston, MA, Health Effects Institute, Diesel Epidemiology Expert Panel; HEI (2000). Health Effects Institute Review of Draft EPA Document: Reconstruction of Teamsters Union Exposures 1950-1999. Boston, MA, Health Effects Institute; HEI (2003). Improving Estimates of Diesel and Other Emissions for Epidemiologic Studies, Baltimore, MD, Dec. 2002, Health Effects Institute.

[38] T. Hesterberg, et al., "A Critical Assessment of Studies on the Carcinogenic Potential of Diesel Exhaust," Critical Reviews in Toxicology, 36, 727-776 (2006).

[39] USEPA 2002 Diesel Health Assessment
at page 5-17.

$\mu g/m^3$ RfC could be considered to be not different from the level of the 15 $\mu g/m^3$ annual $PM_{2.5}$ standard. Thus, based on EPA's evaluation of non-cancer health effects, the ambient annual diesel $PM_{2.5}$ concentrations in California should be without appreciable risk.

In summary, neither the pattern in observational studies nor the findings in controlled exposure studies is consistent with the CARB assumption that diesel $PM_{2.5}$ is equally toxic as generic $PM_{2.5}$. The lack of coherence between the large body of diesel health studies and the CARB assumptions should be acknowledged in the report.

Diesel emissions are already undergoing dramatic reduction throughout California based on a myriad of federal, state, and local control initiatives. The draft methodology is not needed to assure that the progress continues. Since diesel composition is changing dramatically, use of the draft methodology will needlessly alarm the public and may make the efficient use of newer, clean diesels more difficult. This could result in a less efficient transportation system and increased levels of greenhouse gas emissions.

Additional concerns with the CARB assumptions and methodology

The CARB draft points out that cohort studies generally apply proportional hazards models controlling for many individual-level risk factors (such as body mass index, smoking, alcohol use, occupational exposures, age/race, etc. and ecologic factors) before air pollution is considered. However, Moolgavkar[40] pointed out that the Cox proportional hazards model is not the right tool for the detection of small risks in epidemiologic data, particularly in the presence of strong confounders. First, it is highly unlikely that proportionality of hazards would hold throughout the entire period of time covered by these studies. Statistical tests for departures from proportionality of hazards have low power. Even if proportionality of hazards were to hold for exposure to fine PM, we know that it most definitely does not hold for cigarette smoking, a strong risk factor and a potentially strong confounder of the fine PM-mortality association. For example, Moolgavkar notes that we know that, for a given daily level of smoking, the relative risk of lung cancer is strongly dependent on duration of smoking. Moreover, when smokers quit, the relative risk for mortality declines over a period of many years, and not virtually instantly as is assumed by the proportional hazards models. In fact, it is clear from analyses of the ACS I study that proportionality of hazards for cigarette smoking does not hold for lung cancer, cardiovascular, or total mortality (Burns et al. (1996) Table 11).[41] In view of this evidence, one wonders why the Cox model was the primary analytic tool in these studies. This manifestly incorrect model for a strong confounder must bias the estimates of air pollution effects.

Another factor to consider is that in contrast to the chronic mortality studies, there is little evidence of a chronic morbidity signal in the literature. Where effects have been

[40] See D. Menotti and J. Knight, Comments on Proposed "National Ambient Air Quality Standards for Particulate Matter" 71 Federal Register 2620 (Jan. 17, 2006), Docket ID No. EPA-HQ-OAR-2001-0017 April 17, 2006, submitted on behalf of 19 trade associations and attachment thereto by S. Moolgavkar.

[41] Burns DM, Shanks TG, Choi W, Thun MJ, Heath CW, Garfinkel W. The American Cancer Society Cancer Prevention Study I: 12 Year Followup of 1 Million Men and Women. Chapter 3 in Tobacco Smoking Monograph 8, National Cancer Institute, 1996.

reported, it was not possible to attribute the effects to single pollutants or even a specific mix of pollutants. The lack of a strong or consistent chronic morbidity signal is not coherent with the assumption of a strong generic $PM_{2.5}$ chronic mortality signal.

Another limitation in interpreting the cohort studies is that, as the PM CD acknowledges,[42] the appropriate exposure metric for chronic studies is total personal exposure over time, not the level of ambient PM at a central monitor. The CD acknowledges that the major chronic PM studies use long-term average ambient PM concentrations as the exposure metric and do not consider the nonambient component of personal exposure.

However, nonambient exposures contribute to the cohort's total exposure and there is substantial evidence that exposure to nonambient PM is often considerably higher than the exposure to PM from ambient sources. For example, in five studies of personal exposure analyzed by Dominici et al. (2000),[43] the average nonambient contribution to exposure ranged from 29.9 to 85.1 $\mu g/m^3$ for PM10, while the average ambient contribution to personal exposure ranged from 7.7 to 50.7 $\mu g/m^3$. For the five studies, the ratio of nonambient to ambient PM10 contributions ranged from 1.16 to 4.63. Since the participants in these studies primarily were non-smokers, the non-ambient PM exposure is an underestimate of that for the population that includes both smokers and non-smokers. In an extensive study of exposures of inner-city children with asthma in seven communities in the U. S., Wallace et al.[44] report that ambient PM is responsible for only about 25 % of the mean indoor exposures.

As documented in Chapter 5 of the PM CD[45] the exposure to PM of non-ambient origin (i.e., indoor sources) in the U. S. can be substantially higher than that from ambient sources. As noted in the section on air exchange rates, indoor PM sources predominate when air exchange rates are 1.0 or less. As documented in Figure 5-6, measured air exchange rates from a survey of U. S. homes average below 1.0 in 14 of the 16 combinations of region and season. The average air exchange rate was about 0.5. Therefore, indoor sources predominate in most locations and seasons. Thus, if ambient PM is causing a significant mortality and morbidity risk, then the PM from indoor sources would be expected to be causing a substantially larger mortality and morbidity risk.

The CD also indicates[46] that it is not easy to differentiate the role of historic exposure from that of recent exposure in the chronic studies and that the inability to account for exposures prior to enrollment of the cohort hampers interpretation of these studies.

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[42] CD at page 5-119.
[43] Dominici, F; Zeger, S. L.; Samet, J.; A measurement error model for time-series studies of air pollution and mortality, Biostatistics, 2000, 1, 157-175.
[44] Wallace, L. A.; Mitchell, H.; O'Conner, G.T.; Neas, L.; Lippmann, M.; Katten, M.; Koenig, J.; Stout, J. W.; Vaughn, B. J.; Wallace, D.; Walter, M,; Adams,; Liu, L.; Particle concentrations in inner-city homes of children with asthma: the effect of smoking, cooking, and outdoor pollution, Environmental Health Perspectives, 2003, 111, 1265-1272.
[45] Heuss, J.M. ; Alliance of Automobile Manufacturers Comments on the 4th External Review Draft Criteria Document for Particulate Matter. Submitted to CASAC and U. S. EPA, August, 2003.
[46] CD at page 5-118.

Thus, the use of central monitor data from a particular time interval (and ignoring the nonambient exposures) leaves significant potential for exposure misclassification in the chronic studies.

The implications of the strong education effect in the positive chronic studies need to be explored. If the education effect is exposure-related, it changes the PM concentration that is associated with mortality. For example, Rotko et al.[47] evaluated the personal exposures to fine PM for different population sub-groups and reported that less-educated participants had higher exposures than more-educated participants and that different workplace exposures explained most of the difference. Since the ACS and Six-City cohorts were exposed to much higher ambient and workplace exposures in the 1940's 50's and 60's than current exposures would indicate, the possibility that the ACS results represent long-term cohort effects of living and working in historic high coal and industrial pollution areas needs to be considered. Such an explanation might help rationalize the various chronic mortality studies.

Diet and lifestyle differences may also explain the differential risk estimates. For example, Beelen et al. 2008 found suggestive evidence in one of their analyses for higher effects in those with low education and in those with low fruit consumption. Low fruit consumption occurred significantly more in low education households suggesting a possible modifying factor. Beelen et al. speculate that fruit consumption may protect against oxidative stress.

A recent analysis by Janes et al.[48] raises a related important concern. Janes et al. proposed and tested a method for diagnosing confounding bias. They used the approach to estimate the association between monthly averages of fine particles over the preceeding 12 months and monthly mortality rates in 113 U. S. counties from 2000 to 2002. They decomposed the association into two components, one for national trends and the other for local trends. The second component was designed to provide evidence as to whether counties having steeper declines in fine PM also have steeper declines in mortality relative to national trends. They report that the exposure effect estimates are different at the two spatiotemporal scales, which, raises concerns about confounding bias. The authors indicate that they believe the association at the national scale is more likely to be confounded than the association at the local scale. They conclude that " if the association at the national scale is set aside, there is little evidence of an association between 12-month exposure to $PM_{2.5}$ and mortality."

The Janes et al. study strongly suggests that there may be substantial confounding bias in the cohort studies. Although Janes et al found a national association that was similar to that proposed in the CARB report without control for temporal confounding, as they started to control for smooth trends in fine PM and mortality, the evidence changed. The study is important not only because it raises a substantial concern over residual confounding in the cohort studies but also because it is a form of an intervention study.

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[47] Rotko, T.; Koistinen, K.; Hanninen, O.; Jantunen, M.; Sociodemographic descriptors of personal exposure to fine particles ($PM_{2.5}$) in EXPOLIS Helsinki, J. Expos. Analysis and Environ. Epidemiol., 2000, 10, 385-393.

[48] Janes, H.; Dominici, F.; and Zeger, S.; Trends in Air Pollution and Mortality –An Approach to the Assessment of Unmeasured Confounding, Epidemiology, 2007, 18, 416-423.

Janes et al. found that there was no evidence of a positive association between the county-specific rates of change of fine PM and the county-specific rates of change in mortality. Thus, it is a form of real world test as to whether the on-going changes in fine PM that are occurring across the nation are causing changes in mortality. This is exactly the question that CARB is attempting to answer as it develops a methodology for estimating the public health benefits of a given control strategy. Therefore, the draft report should include a careful consideration of the Janes et al. study.

All the issues noted in this section raise additional concerns that the studies CARB is relying on are subject to much greater uncertainty than acknowledged in the draft report.

Despite whatever opinions various experts might hold, the shape of the concentration-response function is not known

CARB assumes that the concentration-response function can reasonably be modeled as linear, and uses cut-offs or thresholds from 2.5 to 7 $\mu g/m^3$. The question of the shape of the concentration-response function was a major consideration during the review of the new PM Criteria Document and the development of the risk assessment included in the PM Staff Paper. Although early drafts of the CD indicated that the PM studies generally show linear concentration-response associations, responding to specific input in CASAC's October 4, 2004 letter, the final CD concludes that "In summary, the available evidence does not either support or refute the existence of thresholds for the effects of PM on mortality across the range of concentrations in the studies."[49] The final Chapter 8 also notes that "the available information does not allow for a clear choice of "threshold" or "no threshold" over the other."[50] This view is consistent with points made by the Special Panel of the HEI Review Committee that recently raised several cautions in interpreting the NMMAPS concentration-response results. They point out[51] that measurement error could obscure any threshold that might exist, that city-specific concentration-response curves exhibited a variety of shapes, and that the use of Akaike Information Criterion may not be an appropriate criterion for choosing between models. The HEI Panel cautioned that lack of evidence against a linear model should not be confused with evidence in favor of it.

CASAC[52] re-iterated its concern in its June 6, 2005 letter noting "The available epidemiological database on daily mortality and morbidity does not establish either the presence or absence of threshold concentrations for adverse health effects." For the risk assessment, CASAC's letter indicates "the Panel favored the primary use of an

[49] CD at page 9-44.
[50] CD at page 8-320.
[51] Health Effects Institute; Commentary on the National Morbidity, Mortality and Air Pollution Study Part III: PM_{10} Concentration-Response Curves and Thresholds for the 20 Largest U.S. Cities, HEI Research Report Number 94, Part III, May 2004.
[52] Henderson, R; Clean Air Scientific Advisory Committee (CASAC) Particulate Matter (PM) Review Panel's Peer Review of the Agency's Review f the National Ambient Air Quality Standards for Particulate Matter:Policy Assessment of Scientific and Technical Information (Second Draft of PM Staff Paper, January 2005); and Particulate MatterHealth Risk Assessment for Selected Urban Areas: Second Draft Report (Second Draft PM Risk Assessment, January 2005), EPA-SAB-CASAC-05-007, U.S. EPA, Washington, DC, June 6, 2005.

assumed threshold of 10 µg/m^3" for both acute and chronic studies along with sensitivity analyses using other threshold assumptions. Therefore, there is no firm basis for choosing a concentration-response function. The concentration-response functions elicited from the experts are no more than personal opinions.

Since there is greater uncertainty in the dose-response function than acknowledged in the draft report, CARB should follow the U. S EPA's procedure and present the results for a wide range of possible cut-off points from background up to 12 or 15 µg/m^3, as shown in Figures 5-28 and 5-29 of the EPA RIA.

A generic ambient fine PM mortality signal is not consistent with the effects of PM exposure in other situations

If low doses of generic ambient particles are causing the serious health effects implied by the statistical associations, then low doses of particles should be causing similar effects in other exposure situations. As discussed above, the exposure to nonambient particles is as high or higher than the exposure to ambient particles. Therefore, there should be a health signal for generic particles as measured by mass in the indoor pollution literature. Although there are well-established indoor health risks from environmental tobacco smoke and from particles of biological origin such as house dust-mite, cockroach, and animal allergens, no substantial or consistent health signal from generic PM has been documented. A recent review of the scientific literature focusing on non-industrial indoor environments looked for evidence of particle health effects.[53] An interdisciplinary group of European researchers surveyed over 10,000 articles by title, chose 1725 abstracts to screen, and chose 70 articles for full review. They concluded that "there is inadequate scientific evidence that airborne, indoor particulate mass or number concentrations can be used as generally applicable risk indicators of health effects in non-industrial buildings." The lack of a health signal from generic indoor PM is not coherent with the assumed presence of a strong outdoor generic ambient PM health signal.

Gamble and Nicolich[54] compared the risks from smoking and occupational exposures with the risks implied by several of the cohort studies and concluded that the toxicity per unit mass of ambient PM would have to be 2 to 4 orders of magnitude higher than that from smoking to explain the ambient risks. The finding led them to conclude that the risks from the cohort studies were not coherent with the risks derived from smoking or occupational studies. Although Pope and Dockery reference Gamble and Nicolich along with other papers in the section on continued skepticism, they do not comment on the calculations or arguments Gamble and Nicolich present.

The findings from massive indoor pollutant exposures in developing nations are also

[53] Schneider, T.; Sundell, J.; Bischof, W.; Bohgard, M.; Cherrie, J. W.; Clausen, P. A.; Dreborg, S.; Kildeso, J.; Kjaergaard, S. K.; Lovik, M.; Pasanen, P.; Skyberg, K.; EUROPART. Airborne Particles in the Indoor Environment. A European Interdisciplinary Review of Scientific Evidence on Associations between Exposure to Particles in Buildings and Health Effects, Indoor Air, 2003, 13, 38-48.

[54] Gamble J. F.; Nicolich, M. J.; Comparison of Ambient PM Risk with Risks Estimated from PM Components of Smoking and Occupational Exposures, J. Air & Waste Manage. Assoc., 2000, 50, 1514-1531.

relevant. Approximately half the world's population relies on unprocessed biomass fuels (wood, coal, crop residues, or animal dung) for cooking and space heating. These fuels are typically burned indoors in simple unvented cookstoves. The exposures to both gases and particles are many times higher than the indoor exposures in developed countries. For example, a detailed exposure study[55] of 55 households in rural Kenya reports that PM10 exposures of adult women (who normally cook and tend the fire) were the order of 5 mg/m^3 while adult male exposures were the order of 1 mg/m^3. These levels are 40 to 200 times higher than the current average U. S. outdoor PM_{10} levels of 25 $\mu g/m^3$. A 2002 World Health Organization report[56] of the health effects of indoor pollution exposures in developing countries reviews the evidence for health effects from these exposures. While there is strong evidence of important effects on acute and chronic respiratory disease in many countries and effects on lung cancer from coal use in China, there is little evidence to date of a strong cardiovascular signal from these massive exposures. This also does not appear to be coherent with the assumption of a strong cardiovascular signal from low doses of generic ambient PM.

Intervention studies do not implicate generic $PM_{2.5}$

The CARB draft and the expert solicitation note the importance of the Clancy et al. intervention study. Intervention studies are very important because they offer an opportunity to evaluate real-world changes that have occurred due to the imposition of controls or other reasons. The Utah Valley studies[57] are an important example of the value of intervention studies but they implicate metals from a closed steel mill, not generic PM. The Clancy et al. and other intervention studies discussed in the CD implicate a variety of pollutants including SO_2 as well as PM and specific PM components. Thus, the available intervention studies do not support a generic $PM_{2.5}$ effect.

There is much greater uncertainty than CARB acknowledges

As a result of all the issues and concerns raised in these comments, it is clear that there is much greater uncertainty than CARB describes and acknowledges in Section V.

In fact, when the first $PM_{2.5}$ standards were set in 1997, the EPA acknowledged that there were unusually large uncertainties associated with establishing standards for PM compared to individual gaseous pollutants. The Agency went on to list nine major areas of uncertainty.[58] The 2005 PM Staff Paper[59] re-iterates the fact that setting air quality

[55] Ezzati, M.; Saleh, H.; Kammen, D. M.; The Contributions of Emissions and Spatial Microenvironments to Exposure to Indoor Air Pollution from Biomass Combustion in Kenya, Environmental Health Perspectives, 2000, 108, 833-839.
[56] Bruce, N.; Perez-Padilla, R.; Albalak, R.; The health effects of indoor air pollution exposure in developing countries, World Health Organization Report WHO/SDE/OEH/02.05, 2002.
[57] Ghio, A.J.; Biological Effects of Utah Valley Ambient Particles in Humans: A Review; J. Aeros. Med.; 2004, 17, 157-164.
[58] U. S. EPA, Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information- OAQPS Staff Paper, EPA-452\R-96-013, U.S. Environmental Protection Agency, Research Triangle Park, NC, 1996.
[59] U. S. EPA, Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information, OAQPS Staff Paper, EPA-452/R-05-005a, December

standards for particulate matter involves unusually large uncertainties relative to setting standards for other single component pollutants.

Pope and Dockery, in their 2006 review, note that one of the reasons for the focus on fine particles is that they can be breathed more deeply into the lungs. The PM CD summarizes a significant body of dosimetry science has been built up based on experiments and computer modeling. For example, Snipes et al.[60] show that particle deposition per unit surface area decreases by orders of magnitude from the extrathoracic to the tracheobronchial and to the alveolar regions. In addition, coarse and fine particles are deposited in both the tracheobronchial and alveolar regions. Thus, Snipes et al conclude that based on dosimetry, the focus should be on PM_{10} not just $PM_{2.5}$.

Because of EPA's previous decision to focus the 1997 PM standards on fine particles, Vostal,[61] based on the Snipes et al study, calculated the mass of fine particles deposited in the alveolar region for both total fine PM and for individual PM components. Vostal showed that actual doses of particles per square centimeter of surface area or per gram of lung tissue were extremely small, the order of fractions of a nanogram of particles (10^{-9} gram) per square centimeter or tens of nanograms per gram of tissue per day for an average ambient concentration of 17.55 $\mu g/m^3$. For PM components, the amounts deposited were correspondingly smaller. These calculations assumed uniform deposition, and it is known that there is heterogeneity in the deposition pattern. In addition, there are differences in deposition between healthy people and those with chronic respiratory disease. However, such differences would increase local tissue levels by modest multiplicative factors, not orders of magnitude. The challenge of PM research is to show how such small deposits can cause the acute morbidity and mortality implied by the statistical associations.

The CARB report should include additional discussion of uncertainties following the example in the EPA Staff Paper and RIA. For example, EPA lists three major sources of uncertainty associated with PM mortality risk. These are:

- The extent to which the effects reported in the long-term exposure studies are associated with historically higher levels of PM rather than the levels occurring during the study period

- The extent to which adverse effects are associated with low-level exposures that occur many times in the year versus peak exposures

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2005, at page 5-71.

[60] Snipes, M; James, A; Jarabek, A; The 1994 ICRP66 Human Respiratory Tract Dosimetry Model as a Tool for Predicting Lung Burdens From Exposures to Environmental Aerosols, Appl. Occup. Environ. Hyg., 1997, 12, 547-554.

[61] Vostal, J; Statistical Associations between Ambient Particulate Matter and Daily Morbidity and Mortality: Can we Identify Mechanisms Responsible for these Health Effects?, in Proceedings of the Air & Waste Management Association's 93rd Annual Conference & Exhibition, Salt Lake City, Utah, June 18-22, 2000, Publ. VIP 97, Air & Waste Management Association, Pittsburgh, PA, 2000.

- The fact that the differential toxicity of specific component species within the complex mixture of PM has not been determined

These major uncertainties should be acknowledged and discussed in the CARB report. In addition, CARB should acknowledge that causality has not been established, that biological mechanisms have not been specifically identified for the presumed effect, and that there are still major uncertainties in the interpretation of the long-term studies related to confounding by other pollutants, life-style factors, and the inappropriateness of the main analytical tool used in these studies. CARB should also acknowledge the major uncertainty associated with the fact that the strength of the presumed mortality effect from generic $PM_{2.5}$ is not consistent with a large body of information on the health effects of particles in other exposure situations. Finally, the report should acknowledge that, to the extent that the associations they are utilizing are not caused by generic ambient $PM_{2.5}$, the benefits that the State expects will not occur.

The methodology for estimating ambient concentrations of $PM_{2.5}$ from diesel-fueled engines has severe limitations

Since the diesel contribution is not directly measured, it must be estimated by indirect methods. Various source attribution techniques have been used in California and elsewhere to estimate the diesel contribution to ambient PM. The CARB draft introduces a new approach which is discussed in detail in Appendix 3. It is introduced as a method to estimate annual average concentrations of diesel particulate matter (DPM) over large spatial scales. The report indicates:

> "It consists of a simple variation of receptor model, which use measurements of ambient chemical concentrations to infer source contributions, known as the tracer species method. A basic assumption in this method is that the ambient concentration of a tracer species, C, may be used alone to infer the ambient concentration of a pollutant from a specific source, S:
>
> $$S = \alpha C$$
>
> where α is a scale factor that is independent of location. In the estimation of DPM, we take C to be the ambient concentration of NOx and S to be the ambient concentration of DPM less than 2.5 µm (DPM2.5). The factor α relates the concentration of PM produced by diesel-fueled engine emissions to the concentration of NOx produced by all sources."

There are several major problems with this approach. NOx is not a unique tracer for diesel emissions in general or for diesel $PM_{2.5}$. There are many sources of NOx in the ambient air. The ratio of DPM/NOx may be similar in many locations across California currently because the current mix of sources is similar. However, as various sources are controlled to a lesser or greater degree over time or as the mix of gasoline and diesel engines in use changes in time or space, the DPM/NOx ratio will change. The draft report discusses several issues with the method. The Engine Manufacturers

Association raised several additional concerns with the proposed approach during the June 25 workshop and recommended a separate review of the methodology for estimating DPM. The need for such a review would be supported by the Alliance of Automobile Manufacturers.

American Enterprise Institute, Joel Schwartz, Sacramento, CA

Comments on the California Air Resources Board's Draft Report "Methodology for Estimating Premature Deaths Associated with Long-Term Exposures to Fine Airborne Particulate Matter in California

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July 11, 2008

This paper provides comments on the California Air Resources Board's (CARB) draft report "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California,"[63] which CARB released for public comment on May 22, 2008.

This update of CARB's methodology for assessing premature mortality due to exposure to fine particulate matter ($PM_{2.5}$) provides an opportunity for CARB to assess the weight of the evidence on the health effects of today's historically low air pollution levels. Unfortunately, rather than provide such an assessment, CARB has selected and structured information in ways that exaggerate harm from air pollution. CARB accepts uncritically the results of studies claiming to find a causal link between air pollution and mortality. On the other hand, CARB stretches for reasons to discount studies that fail to find harm from PM, often misrepresenting these studies in the process. CARB's selective marshalling of evidence creates a false appearance that harm from $PM_{2.5}$ is greater and more certain than is warranted by the actual weight of the underlying evidence from the scientific literature.

CARB's advisory and peer review process only exaggerates the shortcomings in CARB's substantive review of air pollution health science. Despite the wide range of scientific opinion on the validity of observational epidemiology studies and air pollution epidemiology in particular, CARB chose as peer reviewers and scientific advisors epidemiologists who believe strongly in the validity of the methods and results of air pollution epidemiology studies, who are supportive of CARB's regulatory goals, and who have published much of the research CARB and EPA rely on to justify the expansion of their regulatory powers. These selection biases and conflicts of interest ensured that CARB's PM mortality analysis did not receive a genuine critical review by independent experts.

In the remainder of these comments I provide evidence that $PM_{2.5}$ at current and recent levels is not a cause of premature mortality, and show how CARB exaggerated the case

[62] Email address: jschwartz@aei.org.
[63] Hereafter cited as "CARB Methodology."

for harm from $PM_{2.5}$ and shielded itself from independent review.

The Big Picture: Observational Epidemiology Studies Give False Indications of Risk Where No Risk In Fact Exists

CARB's claim that air pollution at current U.S. levels is killing people rests almost solely on results of observational studies—that is, studies with non-randomly selected groups of people and non-randomly assigned exposures. A number of researchers have provided evidence that observational studies are simply not capable of providing reliable information on the existence of small risks, such as those claimed for air pollution.

The implicit assumption in an observational study is that after researchers have controlled for all known non-pollution factors that might be correlated with pollution levels and health outcomes (e.g., weather, smoking, diet, etc.) any remaining correlation between air pollution and health represents a genuine causal linkage between the two. A wide range of evidence shows that this assumption is false and that observational studies tend to "find" effects where no real effects exist.[64]

Indeed, many prominent epidemiologists are wringing their hands over the widespread problem and embarrassment of spurious health claims from observational epidemiology studies and are questioning whether observational studies are even capable of providing valid evidence on health risks.[65]

Unfortunately, this acknowledgement of the limits of observational studies in the wider community of epidemiologists has had little effect on the relatively insular world of air pollution epidemiologists and the regulators who fund them. Even so, there have been some critiques from within air pollution epidemiology. Here, for example, is one caution on the validity of observational studies of air pollution's health effects:

> estimation of very weak associations in the presence of measurement error and strong confounding is inherently challenging. In this situation, prudent epidemiologists should recognize that residual bias can dominate their results. Because the possible mechanisms of action and their latencies are uncertain, the biologically correct models are unknown. *This model selection problem is exacerbated by the common practice of screening multiple analyses and then selectively reporting only a few important results.*[66] (emphasis added)

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[64] S. Begley, "New Journals Bet 'Negative Results' Save Time, Money," Wall Street Journal, September 15, 2006, B1, http://online.wsj.com/article_print/SB115827169620563571.html; J. P. Ioannidis, "Why Most Published Research Findings Are False," PLoS Med 2 (2005): e124; J. P. Ioannidis, "Contradicted and Initially Stronger Effects in Highly Cited Clinical Research," Journal of the American Medical Association 294 (2005): 218-28; G. Taubes, "Epidemiology Faces Its Limits," Science 269 (1995): 164-69; G. Taubes, "Do We Really Know What Makes Us Healthy?" New York Times, September 16, 2007, http://www.nytimes.com/2007/09/16/magazine/16epidemiology-t.html?_r=3&ref=magazine&oref=slogin&oref=slogin&oref=slogin.

[65] S. Ebrahim and M. Clarke, "Strobe: New Standards for Reporting Observational Epidemiology, a Chance to Improve," International Journal of Epidemiology 36 (2007): 946-48; S. J. Pocock, T. J. Collier, K. J. Dandreo et al., "Issues in the Reporting of Epidemiological Studies: A Survey of Recent Practice," BMJ 329 (2004): 883; G. D. Smith and S. Ebrahim, "Epidemiology - Is It Time to Call It a Day?" International Journal of Epidemiology 30 (2001): 1-11; E. Von Elm and M. Egger, "The Scandal of Poor Epidemiological Research," British Medical Journal 329 (2004): 868-69.

[66] T. Lumley and L. Sheppard, "Time Series Analyses of Air Pollution and Health: Straining at Gnats and

The highlighted portion is key. Researchers make many subjective choices in developing statistical models relating air pollution to health. Furthermore, the studies are undertaken by regulatory agencies and air pollution health researchers with the explicit goal of finding harm from air pollution. In this environment, researchers tend to choose statistical models that maximize the effect they "expect" or "hope" to find—a problem known as data-mining. As a result, observational studies become statistical fishing expeditions that turn up chance correlations rather than real effects.

An additional bias is that researchers are more likely to seek publication of, and journal editors are more likely to accept for publication studies that find an effect, while studies that don't find any effects end up packed away into filing cabinets. The result is a problem known as "publication bias." The overall result is that the scientific literature includes lots of studies reporting "effects" that aren't real. Once again, even some air pollution epidemiologists have noted the problem:

> Publication bias arises because there are more rewards for publishing positive or at least statistically significant findings. It is a common if not universal problem in our research culture. In the case of time-series studies using routine data there are particular reasons why publication bias might occur. One is that the data are relatively cheap to obtain and analyse, so that there may be less determination to publish "uninteresting" findings. The other is that each study can generate a large number of results for various outcomes, pollutants and lags and there is quite possibly bias in the process of choosing amongst them for inclusion in a paper. In the field of air pollution epidemiology, the question of publication bias has only recently begun to be formally addressed.[67]

In many areas of health research, randomized trials—a gold standard methodology that reduces or eliminates the biases inherent in observational studies—can be conducted to test claims made based on observational studies. In such cases, observational studies are routinely contradicted when checked against randomized trials, confirming concerns about data-mining and publication bias.[68]

In the case of air pollution, ethical and practical concerns make it impossible to do a randomized trial to test whether today's historically low air pollution levels are deadly. But if observational studies are invalid in all other areas of health research, there's no reason to expect them to do any better on air pollution. In fact, we should expect observational air pollution studies to be even less likely to be valid, because the putative effects they claim to be uncovering are much smaller than in observational studies of medical interventions. As a consequence, the results of observational air pollution

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Swallowing Camels?" Epidemiology 14 (2003): 13-4.

[67] H. Anderson, R. Atkinson, J. Peacock et al., Meta-Analysis of Time-Series Studies and Panel Studies of Particulate Matter (Pm) and Ozone (World Health Organization, 2004), www.euro.who.int/document/e82792.pdf.

[68] Begley, "New Journals Bet 'Negative Results' Save Time, Money."; Ioannidis, "Why Most Published Research Findings Are False."; Taubes, "Do We Really Know What Makes Us Healthy?."

studies are at even greater risk of being statistical figments rather than real effects. Readers of CARB's $PM_{2.5}$ methodology report would have no inkling that the report's conclusions are based on a discredited research methodology. Instead, CARB creates a false impression that observational studies are finding real cause-effect linkages.

Direct Evidence of Spurious Results from Air Pollution Cohort Studies

Although observational air pollution studies in humans can't be checked against randomized trials, we do have some direct evidence that observational studies are producing spurious indications of harm from $PM_{2.5}$. Unfortunately, CARB omits this evidence.

CARB considers the American Cancer Society (ACS) study (also known as the Pope Study) and the Harvard Six Cities (HSC) study to provide strong evidence that any amount of particulate matter in the air is deadly.[69] Both studies assessed the association between long-term $PM_{2.5}$ exposure and risk of death in different cities around the U.S. CARB states "the primary evidence for $PM_{2.5}$ mortality C-R [concentration-response] functions comes from multiple analyses from the Harvard Six Cities study…and the ACS cohort study.[70] In fact, based on the most recent reports from these two studies, CARB has *increased* the estimated risk from $PM_{2.5}$.[71]

However, reanalyses of the ACS and HSC data have demonstrated the extent to which observational studies can give spurious results when researchers leave out important confounding variables. For example, in a reanalysis by the Health Effects Institute (HEI), when migration rates into and out of various cities over time were added to the statistical model relating $PM_{2.5}$ and risk of death, the apparent effect of $PM_{2.5}$ dropped by two-thirds and became statistically insignificant.[72] Migration was just one of several confounding factors that diminished or erased the apparent harm from $PM_{2.5}$, but that were not accounted for by the original researchers.

Regulators and air pollution epidemiologists (including the HEI researchers who did the reanalysis as well as CARB's and EPA's scientific advisors) have ignored this refutation of the ACS/Pope results and continue to claim the ACS/Pope study provides proof of harm from air pollution. When discussing the HEI reanalysis of the ACS/Pope study, CARB claims "the adjusted results did not differ substantively from the original findings. The reanalysis demonstrated the robustness of the PM-mortality risk estimates to many alternative model specifications." This claim is simply false, as several HEI sensitivity analyses showed that the original results suffered from confounding. Once the

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[69] C. A. Pope, 3rd, M. J. Thun, M. M. Namboodiri et al., "Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults," American Journal of Respiratory and Critical Care Medicine 151 (1995): 669-74; C. A. Pope, 3rd, R. T. Burnett, M. J. Thun et al., "Lung Cancer, Cardiopulmonary Mortality, and Long-Term Exposure to Fine Particulate Air Pollution," Journal of the American Medical Association 287 (2002): 1132-41.

[70] CARB Methodology, p. 22.

[71] M. Jerrett, R. T. Burnett, R. Ma et al., "Spatial Analysis of Air Pollution and Mortality in Los Angeles," Epidemiology 16 (2005): 727-36; F. Laden, J. Schwartz, F. E. Speizer et al., "Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study," American Journal of Respiratory and Critical Care Medicine 173 (2006): 667-72.

[72] D. Krewski, R. T. Burnett, M. S. Goldberg et al., Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality (Cambridge, MA: Health Effects Institute, July, 2000).

confounding was corrected, the $PM_{2.5}$ association went away.

CARB ignores other inconvenient results from the HEI reanalysis. For example, in addition to a national average association between $PM_{2.5}$ and mortality, HEI looked at regional variations and reported that $PM_{2.5}$ was not associated with any increase in mortality in California.[73]

The Harvard Six Cities results also turned out to be sensitive to changes in the statistical model. For example, the HSC did not account for differences in physical activity levels among the cities in the study. It later turned out that physical activity and $PM_{2.5}$ levels were inversely correlated, so the ostensible effect of $PM_{2.5}$ could instead have been due to confounding.[74]

The Big Picture: No Harm from $PM_{2.5}$ in Animal Studies

Animal studies provide a further check on the validity of observational epidemiology studies. If air pollution at today's low ambient levels is deadly to people, then we would expect that much higher levels of air pollution would kill at least some laboratory animals. However, researchers have been unable to kill various species of animals even with air pollution at levels many times greater than are ever found in ambient air. A recent review of particulate matter toxicology concluded, "It remains the case that no form of ambient PM—other than viruses, bacteria, and biochemical antigens—has been shown, experimentally or clinically, to cause disease or death at concentrations remotely close to US ambient levels."[75] If high levels of $PM_{2.5}$ can't kill several different species of animals, it's unlikely that low levels of $PM_{2.5}$ are killing people.

CARB implies that Sun et al. (2005) provides direct toxicological evidence of harm from $PM_{2.5}$ at real-world ambient levels.[76] Sun et al. claimed to have uncovered a direct cause-and-effect relationship between current $PM_{2.5}$ levels and heart disease, especially along with a high-fat diet, based on a study of mice. Both researchers and the media hailed this study as providing proof, previously lacking in animal studies, that air pollution is causing heart disease, and therefore premature death, in humans.

In fact, the Sun et al.'s study had nothing to do even with real mice, much less with people. Sun et al. used mice genetically engineered to be lacking a blood lipid/cholesterol regulation system. These mice had 14 times the cholesterol levels of normal mice. For comparison, only about one in 500 American males has cholesterol of even twice the national average and virtually no human has cholesterol greater than four times the average. The very reason for using such unrealistic mice is that even massive $PM_{2.5}$ doses don't cause heart disease in normal mice. In addition, although

[73] See Figure 21, p. 197 of the HEI report. Note that relative risks were below 1.0 (i.e., no increase in mortality due to $PM_{2.5}$) in all of California. Ibid.

[74] F. W. Lipfert, "Estimating Air Pollution-Mortality Risks from Cross-Sectional Studies: Prospective Vs. Ecologic Study Designs," Health and Regulatory Issues, Proceedings of the International Specialty Conference, Air and Waste Management Association, 1995.

[75] L. C. Green and S. R. Armstrong, "Particulate Matter in Ambient Air and Mortality: Toxicologic Perspectives," Regulatory Toxicology and Pharmacology 38 (2003): 326-35.

[76] CARB Methodology, p. 17. Q. Sun, A. Wang, X. Jin et al., "Long-Term Air Pollution Exposure and Acceleration of Atherosclerosis and Vascular Inflammation in an Animal Model," Journal of the American Medical Association 294 (2005): 3003-10.

the researchers claimed their $PM_{2.5}$ doses were similar to real world doses, the acute doses were in fact substantially higher than even the highest real world exposures.[77]

CARB Mischaracterizes Cohort Studies that Do Not Find Harm from $PM_{2.5}$

Two cohort studies did not find harm from $PM_{2.5.}$ Rather than contend with this evidence against harm from $PM_{2.5}$, CARB instead mischaracterizes the studies' methods and results, creating a false impression that the studies are irrelevant or invalid.

The Veterans study assessed the association between $PM_{2.5}$ and mortality risk from 1976-2001 in a cohort of 70,000 male U.S. veterans with high blood pressure.[78] The study reported that higher $PM_{2.5}$ was associated with a statistically significant *decrease* in risk of death.

CARB claims "Overall, in the VA analyses, effect estimates to various measures of PM were unstable and not robust to model selection, time windows used, or various other analytic decisions."[79] Even if this were true, the criticism applies equally to the ACS/Pope and Six Cities cohorts. As already noted, in the ACS/Pope cohort the ostensible effect of $PM_{2.5}$ disappeared when additional confounding factors were considered, including migration, sulfur dioxide, and several others. The ACS/Pope results also feature several biologically implausible results. For example, $PM_{2.5}$ appeared to kill men, but not women; those who said they were moderately active, but not those who said they were very active or sedentary.[80] These biologically implausible patterns suggest the correlation of $PM_{2.5}$ and mortality was a statistical figment rather than a real causal effect.

The most recent report on the ACS/Pope cohort also reports results that are "not robust to model selection." CARB highlights Jerrett et al. (2005) because it ostensibly found greater risks from $PM_{2.5}$ than were reported in the original ACS/Pope studies.[81] CARB ignores the fact that the relative risk from $PM_{2.5}$ became statistically insignificant in the models that had the most extensive controls for confounding.

In any case, the Veterans results are not in fact unstable. The study has consistently found that higher $PM_{2.5}$ is associated with either no mortality or lower mortality. The Veterans study did however find that whatever the effects of $PM_{2.5}$, they are decreasing with time. Perhaps CARB mistook this decline for "instability." Ironically, the ACS/Pope study also suggests that $PM_{2.5}$ effects are decreasing with time (though Pope et al.

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[77] For a more detailed demonstration of why Sun et al. is irrelevant for assessing health risks in mice or people see J. Schwartz, Air Pollution and Health: Do Popular Portrayals Reflect the Scientific Evidence? (Washington, D.C.: American Enterprise Institute, May 2006), http://www.joelschwartz.com/pdfs/AirPoll_Health_EPO_0506.pdf.

[78] F. W. Lipfert, J. D. Baty, J. P. Miller et al., "PM2.5 Constituents and Related Air Quality Variables as Predictors of Survival in a Cohort of U.S. Military Veterans," Inhalation Toxicology 18 (2006): 645-57; F. W. Lipfert, H. M. Perry, J. P. Miller et al., "The Washington University-EPRI Veterans' Cohort Mortality Study," Inhalation Toxicology 12 (suppl. 4) (2000): 41-73; F. W. Lipfert, R. E. Wyzga, J. D. Baty et al., "Traffic Density as a Surrogate Measure of Environmental Exposures in Studies of Air Pollution Health Effects: Long-Term Mortality in a Cohort of Us Veterans," Atmospheric Environment 40 (2006): 154-69.

[79] CARB Methodology, p. 8.

[80] Pope, Burnett, Thun et al., "Lung Cancer, Cardiopulmonary Mortality, and Long-Term Exposure to Fine Particulate Air Pollution."

[81] Jerrett, Burnett, Ma et al., "Spatial Analysis of Air Pollution and Mortality in Los Angeles."

never say so explicitly).

For the 1982-89 follow-up period, Pope et al. (1995) reported a nationwide average relative risk (RR) of 1.069 per 10 □g/m^3 $PM_{2.5}$. However, for the 1982-98 follow-up period Pope et al. (2002) reported an RR of 1.04. Although the authors never say so explicitly, this means that the RR declined between the 1982-89 and 1990-98 follow-up periods. Based on data provided in the two papers, one can calculate that the RR for 1990-98 was about 1.019, and is statistically insignificant. Thus, even on its own terms, the ACS/Pope study suggests that any harm from $PM_{2.5}$ that might have existed 20 or 30 years ago has now disappeared.

CARB also discounts the Veterans study based on the claim that the cohort is not representative of Californians. CARB states "As our objective is to derive a relative risk applicable to the general population of California, it is important to use studies that have a similar at-risk population. This criterion would eliminate direct application of studies like the Washington University-EPRI Veterans Cohort…which focused on male military veterans under treatment for hypertension, with 81 percent current or former smokers."[82]

CARB's objection is particularly ironic because the Veterans cohort has exactly the characteristics CARB would normally look for in an air pollution health study. It has the largest percentage of minorities of any cohort in an air pollution mortality study (35 percent African American). The high minority component dovetails with CARB's goal of ensuring that air pollution doesn't disproportionately harm minorities.

The men in the cohort also had high blood pressure, which should have made them *more* susceptible to any harm from air pollution, when compared with the general population. CARB's goal is to set standards that protect even the most "sensitive" groups, and the Veterans cohort *is* a sensitive group. Instead, CARB focuses on the mainly white, middle class ACS cohort and on the Harvard Six Cities cohort, which did not even include people in California.

CARB also gives short shrift to Enstrom (2005), which reported on the association of $PM_{2.5}$ and mortality in cohort of 36,000 elderly Californians from 1973-2002.[83] The study found that $PM_{2.5}$ was not associated with any increase in mortality risk after the early 1980s. In discounting the Enstrom results, CARB states "the Enstrom (2005) study of elderly Californians neither adequately controlled for smoking nor adjusted for exposure to environmental tobacco smoke, two factors that could significantly alter the effect of PM exposures on premature death. Further, exposure misclassification is another issue of concern. In Entrom's [sic] study, $PM_{2.5}$ was assigned on the basis of data from just a few monitoring sites and at times on very few measurements (Brunekreef 2006). No discussion was provided as to the representativeness of sites."[84]

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[82] CARB Methodology, p. 21.
[83] J. E. Enstrom, "Fine Particulate Air Pollution and Total Mortality among Elderly Californians, 1973-2002," Inhalation Toxicology 17 (2005): 803-16.
[84] CARB Methodology, p. 22.

CARB cites a letter to the editor by Brunekreef and Hoek (2006) to support its discounting of Enstrom.[85] But Brunekreef and Hoek's claims are either mistaken or apply equally well to studies that claim to find harm from $PM_{2.5}$. For example, CARB says of Enstrom (2005) "$PM_{2.5}$ was assigned on the basis of data from just a few monitoring sites and at times on very few measurements." In fact, Enstrom used data from the Inhalable Particulate Network (IPN), a special $PM_{2.5}$ monitoring network EPA set up during 1979-83. These are the only data on $PM_{2.5}$ available from that time. Furthermore, *the Pope/ACS study used this exact same IPN data*. Thus, if Enstrom's study is invalid because of problems with the $PM_{2.5}$ data then the ACS/Pope study is likewise invalid. Indeed, one could level the same critique at the Harvard Six Cities study, which set up $PM_{2.5}$ monitors especially for the study, but only one monitor per city.

CARB is also incorrect in claiming that Enstrom did not adequately control for smoking. Enstrom included controls for smoking status both at study entry in 1959 and in 1972, just before the follow-up period began. Enstrom did not adjust for exposure to environmental tobacco smoke, but as he points out "No control for environmental tobacco smoke (ETS) was necessary because a separate study showed that ETS was not related to mortality among the never smokers in this cohort."[86]

CARB also asserts of Enstrom (2005) "Yet another issue is the long time passed since enrollment (1959) and follow-up (1973- 2002), which must have been associated with many changes in diet, smoking, occupation, etc., factors for which the authors could not adequately control." This claim is misleading. Smoking status was ascertained not only at entry to the study in 1959, but also in 1972 at the beginning of the follow-up period. Smoking is the single largest factor affecting health and CARB is simply mistaken in claiming that Enstrom did not control for it.

CARB's criticism also applies equally well to the cohort studies that CARB lauds. In the Pope/ACS study, the controls for smoking, diet, etc. were based on data collected at entry to the study in 1982. Thus, this study also fails to capture any changes in status or behavior that occurred after entry to the study.

CARB's critique of Enstrom is also an extreme case of selective citation. Although CARB cites Brunekreef and Hoek's (2006) critique of Enstrom (2005), CARB omits Enstrom's response, which refutes Brunekreef and Hoek's claims.[87]

Overall, CARB stretches for ways to discount the results of studies that fail to find harm from $PM_{2.5}$, while ignoring the shortcomings and inconsistencies of studies that do claim to find harm from $PM_{2.5}$. In the final version of the report, CARB must do a far better effort of providing realistic and honest reviews of the evidence, regardless of whether than evidence is congenial to CARB's bureaucratic interests.

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[85] B. Brunekreef and G. Hoek, "A Critique Of "Fine Particulate Air Pollution and Total Mortality among Elderly Californians, 1973-2002" By James E. Enstrom," Inhalation Toxicology 18 (2006): 507-8.
[86] J. E. Enstrom, "Response To "A Critique of 'Fine Particulate Air Pollution and Total Mortality among Elderly Californians, 1973-2002" by Bert Brunekreef, PhD, and Gerard Hoek, PhD," Inhalation Toxicology 18 (2006): 509-14.
[87] Ibid.

EPA's Expert Elicitation Should Not Be Taken Seriously

EPA recently completed an "Expert Elicitation" on particulate matter health effects.[88] The Expert Elicitation included 12 scientists, most with expertise in air pollution epidemiology and others with expertise in toxicology and medicine. The experts reviewed a wide range of studies on air pollution and health and sat for several hours of interviews during which they gave their expert opinions on the health effects of particulate matter air pollution, and in particular their opinion on the exposure-response relationship between PM levels and risk of premature mortality. CARB places great weight on Expert Elicitation's results, concluding "In summary, it is appropriate to rely on the U.S. EPA experts' judgments for California's specific risk assessments."[89]

Both EPA and CARB create the impression that the scientists EPA chose for the expert elicitation provided an independent and unbiased evaluation of PM health effects. But the Expert Elicitation was in fact vitiated by selection biases and conflicts of interest. CARB states that the "Experts relied upon a core set of cohort epidemiology studies to derive their quantitative estimates, mainly those associated with the ACS [American Cancer Society] and [Harvard] Six Cities cohorts."[90] But of the 12 experts, six are co-authors of these studies, meaning they were giving their expert opinion on their own research.[91] One of the experts is the chief air pollution epidemiologist at the California Environmental Protection Agency. Most, perhaps all of the researchers are heavily funded by EPA and/or CARB to do the research that EPA and CARB then use to justify expansion of their regulatory authority. Among epidemiologists skeptical of a link between low-level and pollution and mortality, none were included in the Expert Elicitation.

Clearly, the Expert Elicitation did not come close to providing independent and unbiased analysis. Rather, the study design inherently ensured that it would confirm EPA's preconceptions and regulatory goals, rather than uncover realistic information on air pollution health effects. The Expert Elicitation is not an appropriate guide upon which to make scientific judgments or inform regulatory policy and CARB should remove the Expert Elicitation's results from the Methodology report.

CARB Should Commission Genuinely Independent Reviews of Its Analysis

CARB's own advisory and peer review process suffers from a similar lack of independence and conflict of interest. To ensure that CARB's report receives a genuine critical evaluation before its release, CARB should include among its advisors and peer

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[88] Industrial Economics, Expanded Expert Judgment Assessment of the Concentration-Response Relationship between $PM_{2.5}$ Exposure and Mortality, prepared for the U.S. Environmental Protection Agency (Washingon, D.C.: September 21, 2006); H. A. Roman, K. D. Walker, T. L. Walsh et al., "Expert Judgment Assessment of the Mortality Impact of Changes in Ambient Fine Particulate Matter in the U.S," Environmental Science and Technology 42 (2008): 2268-74.

[89] CARB Methodology, p. 23.

[90] CARB Methodology, p. 17.

[91] For example, of the 12 experts, C. Arden Pope, Daniel Krewski, Kazuhiko Ito, and George Thurston authored papers on the ACS study. Joel Schwartz, Douglas Dockery, and Pope authored papers on the Harvard Six Cities study.

reviewers (1) epidemiologists who have provided evidence against the existence of a causal association between air pollution and mortality, (2) epidemiologists who have evaluated the validity of observational methods for assessing the existence of small risks, and (3) researchers who are not air pollution epidemiologists, but who are expert in the mathematical techniques used in air pollution epidemiology, and of assessing the real-world validity of causal inferences based on those techniques—for example, econometricians, statisticians, and researchers in other sub-fields of risk factor epidemiology.

EPA's Expert Elicitation and CARB's advisory and review process are cases of the emperor asking his tailors to judge the quality of his clothes. It is time for the emperors of air pollution regulation to expand their circle of advisors.

Additional Errors and Mischaracterizations Dutch cohort study.
According to CARB, even studies that find no harm from PM, nevertheless lend support to CARB's claim of a PM-mortality link. Here is CARB's description of results from a Dutch study of PM and mortality:

> A more recent study on the same [Dutch] Cohort, Beelen et al. (2008), reinforces the conclusions of the pilot study. The authors found a positive association between traffic intensity on the nearest roadway to the subject's residence and death rate. They also confirmed the link between interpolated BS [black smoke] concentrations and cardiopulmonary mortality. *While the associations between pollutants and mortality in this study were not statistically significant, the authors' methodology was very careful, and their results lend convincing support to the link between premature death and PM.* [92] [emphasis added]

In other words, Beelen et al. did not find a statistically significant association between particulate matter and mortality and CARB believes Beelen et al. used a "very careful" methodology. Yet CARB still claims that this study "lend[s] convincing support to the link between premature death and PM."

CARB should adjust its Methodology report to reflect the lack of support for $PM_{2.5}$ effects in this study.

Dublin coal-ban study. The city of Dublin, Ireland in 1990 banned to use of soft (bituminous) coal for home heating and cooking, which resulted in a large drop in black smoke levels, particularly in winter. A study in the *Lancet* concluded that the coal ban caused a reduction in premature mortality.[93] CARB singles out this report as an intervention study that provides evidence that declines in $PM_{2.5}$ cause declines in mortality.

The Dublin study clams to demonstrate that premature mortality decreased due to PM reductions that resulted from Dublin's ban on the burning of bituminous coal on

[92] CARB Methodology, p. 8.

[93] L. Clancy, P. Goodman, H. Sinclair et al., "Effect of Air-Pollution Control on Death Rates in Dublin, Ireland: An Intervention Study," Lancet 360 (2002): 1210-4.

September 1, 1990. However, there was a large spike in mortality in winter 1990, just before the ban went into effect. This could have created the appearance that the drop in mortality after the coal ban was due to the reduction in black smoke due to the coal ban, even if the coal ban had nothing to do with it.

The authors controlled for flu outbreaks in their model using an indicator variable, and one of the five flu outbreaks during the study period did occur during winter 1990. But it is clear from the data that the mortality spike is not mainly a result of the flu outbreak. First, the winter 1990 mortality spike occurred for all causes of death, whereas only cardiovascular and respiratory deaths were anomalously high during other flu outbreaks. Second, the winter 1990 mortality anomaly was much greater than during other flu outbreaks.[94]

Even if the Dublin results are taken to have found a causal relationship between lower air pollution and fewer deaths, it's not clear that it has any lessons for air pollution in California. First, the study was based on black smoke levels in Dublin, which went from winter-average levels of 85 $\mu g/m^3$ before the coal ban down to 22 $\mu g/m^3$ after. Annual-average levels went from 50 $\mu g/m^3$ down to 15 $\mu g/m^3$. These are for black smoke alone, rather than total $PM_{2.5}$, so total $PM_{2.5}$ levels would have been even higher. The study is thus based on much higher average $PM_{2.5}$ levels than the levels of the federal or California $PM_{2.5}$ standards.

In addition, the study used outdoor black smoke levels as the exposure variable. But the coal was being used for home space and water heating. Indoor PM exposures would therefore have been much higher than even the already-large outdoor exposures, further increasing the exposure levels when compared with current U.S. standards, especially given that people spend most of their time indoors, especially during winter when indoor $PM_{2.5}$ levels would have been highest.

Overall, the Dublin study isn't all CARB cracks it up to be and in any case is irrelevant for PM levels and routes of exposure in California. CARB's Methodology report should be adjusted to reflect this.

CARB Must Go Back to the Drawing Board

Before finalizing the Methodology report, CARB must consider the full weight and strength of the evidence, including evidence against causal associations of air pollution and mortality, weaknesses in the studies that purport to demonstrate a causal connection, and evidence on the fundamental validity of the methods used to make causal claims. Furthermore, CARB must take these steps within a framework that includes genuinely independent scientists both from within and outside air pollution epidemiology.

In order to ensure that CARB's estimate of $PM_{2.5}$ health effects reflects the real-world validity of $PM_{2.5}$ studies, and the real-world likelihood of harm from current, historically

[94] It is also worth noting that the authors didn't actually have any data on flu outbreaks in Ireland. Instead, they assumed that a flu outbreak was occurring in any 14-day moving window in which the national mortality rate due to influenza or pneumonia was above the 95th percentile.

low levels of $PM_{2.5}$, I offer the following recommendations:

1. CARB should step back and assess whether observational epidemiology studies are capable of providing reliable information on the existence of small risks.
   Observational studies are the main justification for the claim of a causal association between air pollution and premature death, but they are also the weakest form evidence.
   As shown in these comments, there is good reason to discount the results observational studies, due to the inherent weaknesses and biases in the methods themselves, and due to the clear influence of data mining and publication bias. These factors work to inflate apparent harm from air pollution. In addition, experimental studies with both humans and animals don't support a causal air pollution-mortality association, contradicting the observational studies.
   There are thousands of observational studies claiming to provide support for a causal association between low-level air pollution and risk of death. But implementing invalid techniques over and over again doesn't improve their validity.

2. CARB should not to omit or mischaracterize contrary evidence, and should take a more critical look at studies claiming to support a causal association between air pollution and mortality. My comments provide a few examples of such omissions and mischaracterizations, but there are many more.

3. EPA's Expert Elicitation suffers from serious biases and conflicts of interest that render it's results invalid. CARB should not base its conclusions about the health effects of $PM_{2.5}$ on the Expert Elicitation and should not give the Expert Elicitation a prominent role in its Methodology report.

4. CARB's analysis suffers from biases and conflicts of interest similar to those of EPA's Expert Elicitation. To ensure that CARB's report receives a genuine critical evaluation before its release, CARB should include among its advisors and peer reviewers (1) epidemiologists who have provided evidence against the existence of a causal association between air pollution and mortality,[95] (2) epidemiologists who have evaluated the validity of observational methods for assessing the existence of small risks,[96] and (3) researchers who are not air pollution epidemiologists, but who are expert in the mathematical techniques used in air pollution epidemiology, and of assessing the real-world validity of causal inferences based on those techniques—for example, econometricians, statisticians, and researchers in other sub-fields of risk factor epidemiology.[97] CARB needs a broad range of views and expertise to ensure that its results reflect the weight of the evidence rather than merely CARB's bureaucratic interests.

5. Putting aside the fundamental concerns about whether estimates based on observational studies represent real risks, it is important to find out why different researchers come up with such different results for $PM_{2.5}$ effects.
   To find out what is causing all of these different results, CARB should commission

[95] For example, Fred Lipfert, James Enstrom, Suresh Moolgavkar, Lise Tole, William Keatinge, and Richard L. Smith to name just a few.
[96] For example, George Davey Smith, John Ioannidis, or members of the STROBE team.
[97] For example, Michael Greenstone, David Freedman, Paul Switzer, Anne Smith, as well as researchers mentioned in the previous footnote.

reanalyses to confirm that the original results can be replicated and to determine how robust and reliable the various results are to different specifications and approaches.

At least two separate researchers should perform these reanalyses; at least one “skeptic” and at least one “believer.” Having researchers with different points of view will ensure vigorous testing and review of the validity of any given approach to analyzing the data.

Outside statisticians, econometricians and epidemiologists should also be part of the reanalyses themselves, as well as up-front reviewers of the reanalysis protocols as well as peer-reviewers of the results.

The Methodology report’s errors and biases are too extensive and profound for the report to merely be tweaked and released in a few weeks, as the current schedule requires. Instead, CARB must go back to the drawing board by appointing genuinely independent scientific advisors and peer reviewers, commissioning genuinely independent reanalyses of key data, and rewriting the report from scratch.

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July 11, 2008

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Re: Comments on the draft: **Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California**

Dear Dr. Tran,

BNSF Railway is providing comments prepared by ENVIRON International Corporation (ENVIRON) on the Air Resources Board (ARB) draft report, ***Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California.***

With the release of this draft report, ARB has completed a revised assessment of human health effects attributed to air pollution associated with goods movement. The current revision was prepared, at least in part, as a response to a critical evaluation elicited by ARB of the methods used and documentation provided in previous versions of health effects assessments for goods movement activities. The current ARB document includes reviewers' evaluations as Appendix 1.

With respect to previous ARB analyses that linked premature mortality to goods movement activities, ENVIRON has expressed concerns that documentation of rationale, methods, and data sources was not sufficient to support peer review. With some exceptions, the documentation concerns have been addressed in the current

report. Additionally, ARB is to be commended for extending their review of the epidemiological literature to include more recent, relevant publications; for more fully describing their assessment of the quality and applicability to California of the epidemiological literature they reviewed; for considering alternatives to the linear, no threshold exposure-response relationship; and for acknowledging and in part attempting to quantify the uncertainty associated with their calculated estimates.

In spite of these improvements in ARB's assessment and its documentation, several concerns persist regarding the current ARB risk assessment and risk attribution effort. Our comments on this effort address three key subject areas (1) epidemiologic concepts and data, (2) policy implications, and (3) methodology used to estimate ambient concentrations of particulate matter from diesel-fueled engine emissions. Our comments related to epidemiology and policy are provided in this letter, while those that address the estimation of particulate matter from diesel-fueled engines are provided as Appendix 1.

Epidemiological concepts and data used by the ARB

The approach that underlies the attribution of a specific number of deaths to air pollution associated with goods movement is based on the epidemiological concept of "attributable risk", which relies implicitly on a number of assumptions. Some of these underlying assumptions have been addressed by ARB in the current report, while others were not. The following comments are not meant to represent a comprehensive discussion of the assumptions underlying the concept of attributable risk, but focus on selected points that are critical to the validity of ARB's conclusions.

> Assumption 1: Effect estimates from epidemiological studies conducted in one population and location can be validly applied to other populations and locations.
>
> For this assumption to hold it would be necessary, among other things, for the studied population, exposure levels and disease(s) to be comparable to the target population, exposure levels and the disease(s) for which attributable risks are to be calculated. The location is of importance not only to account for differences in the sociodemographic and even genetic composition of the populations, but also to account for differences in pollution constituents that are determined by land use and land cover – including geological and constructed features – of the areas being compared. Furthermore, weather patterns, seasonality and vegetation may contribute to important differences that may limit the applicability of study results.
>
> The current ARB health risk assessment (HRA) discussed the need for the studied population, location, exposure and outcome to be similar to the population, location, exposure and outcome of interest, i.e., residents of specific areas in California exposed to diesel particulate matter <2.5 microgram per cubic meter ($\mu g/m^3$) emitted as a result of goods movement activities and premature deaths. The ARB did not offer convincing arguments that the key epidemiological studies selected to provide risk estimates could, in fact, be generalized to the specific California populations of interest, their exposures or

their outcomes. In particular, page 22 of the ARB report notes:

> "National-scale epidemiological studies addressing short-term effects of PM exposures using time-series analyses do not demonstrate an appreciable difference between California and other states or regions in relative risks. For example, in a publication on 91 U.S. cities addressed by the National Mortality Morbidity Air Pollution Study, Dominici et al. (2005) showed that the southern California relative risk was slightly higher than the national average, while that of the Northwest (which included northern California as well as Oregon, Washington) was slightly lower than the national average. A simple average of the southern California and Northwest relative risks gives a value almost identical to the national average. A recent publication investigating PM2.5 mortality in 27 large communities around the U.S. (Franklin et al. 2007) found that the C-R function was above the national average for San Diego and Sacramento but below the national average and insignificant for Riverside and Los Angeles. It should be noted that the cohort study by Jerrett et al. (2005) did find a statistically significant effect for the Los Angeles metropolitan area, once exposure was estimated with more geographic precision. Thus, the available evidence does not provide any rationale for excluding relative risks derived from studies across the U.S. to California."

In fact, no such conclusion can be drawn based on the studies cited in the preceding paragraph. These statements by ARB actually highlight considerable geographic variability, even within California, and the importance of "geographic precision" in selecting study results to be applied to the populations and regions of interest to the ARB rather than applying national study results to all areas in California. The importance of geographic specificity in assessing the health risks associated with pollution is supported by the analysis of Janes et al. (2007) showing that 90% of the variability in the association between air monitoring data and total mortality measured at the national level (U.S.) for 2000-2002 was explained by the between-county variance.

<u>Assumption 2</u>: The association between $PM_{2.5}$ and mortality is constant over time, and the temporal trends are the same nationally and locally.

The Janes et al. (2007) analysis also evaluated county-level vs. national temporal trends in the association between monitored $PM_{2.5}$ and total mortality. The authors found that county-specific temporal trends were generally not similar to national temporal trends, and that Los Angeles County was among the three counties whose temporal trends differed most dramatically from national temporal trends. Specifically, $PM_{2.5}$ increased in Los Angeles County relative to the national trend in $PM_{2.5}$, while all cause mortality decreased in Los Angeles County relative to national death rates.

<u>Assumption 3</u>: If the population, location, exposure and outcome differences discussed above can be accounted for, then it is possible to attribute a specific

number of health outcomes to a specific air pollution constituent, such as $PM_{2.5}$ due to diesel emissions.

It is not valid to calculate a specific number of deaths at a specific site due to specific air pollution constituents, even if the calculation inputs are based on data for the same population and location. Such calculations are based on unsupported, but inherent, assumptions that the relationships between individual pollutants and the health outcome are independent of all other risk factors for the same disease in the target population, and are directly causal. Such oversimplification of this concept and its application can lead to invalid conclusions. This is especially true if one attempts to attribute $PM_{2.5}$ from a single source or several nearby sources.

Assumption 4: Removal of one identifiable constituent of air pollution (i.e., the diesel-specific particulate matter component of "air pollution") is possible, and will result in a proportionate decrease in the number of deaths due to exposure to air pollution measured in the composite.

There is no scientific evidence that elimination of any specific, individual air pollution constituent, even if that were possible, would result in the prevention of the estimated number of deaths. The methods for calculating the number of deaths prevented are not validated; and, where the methods have been applied in similar situations they do not perform well. As an example, consider the discussions provided by Rockhill et al. (1998) regarding risk factors for breast cancer, and by Levine (2007) regarding obesity-related diseases. Problems with the attributable risk methods, as they are widely (mis)applied and (mis)interpreted, arise in the current setting as a result of the arguments above regarding the specificity of the association between air pollution constituents and death, the complexity of the air pollution mixture, the interactions between air pollution constituents, and the multiple and interacting causes of death that exist. It should also be noted that attribution of risk is based on measures of correlation., Most correlations reflect complex associations between constellations of risk factors and health outcomes, and cannot be interpreted as causal, even if the specific risk factor of interest plays some role in disease risk.

Aside from the faulty assumptions underlying the attributable risk calculations, BNSF is concerned by ARB's reliance on un-validated quantitative estimates of numbers of deaths due to diesel particulate matter arising from goods movement, or avoided by reductions in diesel particulate matter from new controls on goods movement. Specifically, although the methods employed by ARB in previous goods movement assessments have been improved by the inclusion of confidence intervals and uncertainty ranges, the "bottom line" of the risk assessment is still represented by a numerical estimate of a number of deaths attributed to diesel particulate matter from goods movement. BNSF notes that the underlying methods are not valid and thus can not produce valid estimates of numbers of deaths. Furthermore, BNSF believes that ARB will not be well-served by promulgating these estimates. For example, if ARB is correct that their calculations underestimate the number of premature deaths attributable to diesel particulate matter, then the use of these estimates virtually insures

that any improvement in air quality resulting from the implementation of new controls on goods movement will be perceived as inadequate, because the predicted number of deaths avoided by a specific level of improvement in air quality cannot be achieved. Conversely, if the ARB calculations overestimate the number of premature deaths attributable to diesel particulate matter, then any assessment of the effectiveness of new emissions controls will be overstated. Additionally, the use of any attributable risk calculation depends on the unsupported assumption that population aggregate risks remain stable over time. To the extent that population-level risks vary over time, the result of an attributable risk calculation will not be informative in assessing the efficacy of an intervention such as emissions controls (i.e., regulatory impact analysis).

In addition to the conceptual concerns discussed above, we also note that:

- In discussion of the limitations of their work, the ARB described ways in which their calculations might underestimate the true number of deaths attributed to diesel particulate matter. However, ARB did not acknowledge the possibility that their calculations resulted in overestimates of adverse effects attributable to diesel particulates. The ARB should do so.

- Premature mortality is not defined in the report; the definition must be provided. Additionally, the ARB should document whether premature mortality was defined consistently across the key studies, and whether the study definitions in turn were consistent with ARB's own definition.

- Baseline mortality is not defined in the report. For example, ARB needs to clarify whether accidental deaths were included in the baseline mortality incidence data as is implied in the current discussion.

- The Center for Disease Control (CDC) website cited by ARB as the source of baseline mortality incidence rates does not have mortality data for the age categories or census tract areas reportedly used by ARB. The report needs to clarify whether CDC data were in fact used, if they were used with modification, or if there is some other data source for these rates.

BNSF requests an opportunity to further comment on the study once this critical information has been provided.

Policy Implications of the ARB Report

<u>Policy Concern 1</u>: The methods and results contained within the ARB report should be used as a guide for policy makers, not as a *de facto* regulation.

The ARB report and the methods and conclusions contained within it were developed to support future regulatory efforts to lower statewide $PM_{2.5}$ concentrations. Although the methods have not been incorporated into regulation(s), we are concerned that they may have reached *de facto* regulatory standing with the ARB. Estimates of premature mortality from diesel particulate matter (DPM) have been incorporated by the ARB into HRAs of California's rail

yards, the combined Ports of Los Angeles and Long Beach, and the West Oakland Community even though the methodologies have not been subjected to required administrative and public review and adherence to promulgation requirements. It is not appropriate for a state agency to require application of and adherence to a specific method of health effects assessment outside of the regulatory process, especially when those expectations target a specific industry. To do so means that the burden of compliance falls on that industry without benefit of legislative review, and without guidance to support consistent compliance and implementation efforts.

Policy Concern 2: The ARB has not defined a *de minimis* level of premature mortality.

The ARB has neither analyzed nor made a determination of the number of hypothetical premature deaths deemed to be significant. Eliminating all potential premature deaths estimated from presumed exposures to $PM_{2.5}$ is not practical or achievable, yet without stated policy or scientific guidance from the ARB, the significance of hypothetical premature mortality calculations cannot be interpreted. By comparison, many federal environmental laws and regulations have applied the concept of *de minimis* risk (i.e., that level of hypothetical risk that is so small that is not considered significant or worthy of attention [Cohrssen and Covello, 1989]). Absent a comparable determination from ARB (i.e., of the *de minimis* number of premature deaths), ARB leaves industry, local regulatory agencies, and the public without guidance to interpret the significance of hypothetical premature mortality calculations.

Related to these concerns is that incorporation of ARB's hypothetical premature mortality methodology into California Environmental Quality Act (CEQA) analyses will require interpretation of a significance threshold, as well as what level of hypothetical premature deaths constitutes a cumulatively significant finding. Again, ARB provides no guidance on this, leaving interpretations to be made by those without qualification to perform the analysis.

Policy Concern 3: The ARB report concludes that premature mortality may occur at concentrations below the current California standard of 12 $\mu g/m^3$ and may occur at or near background levels of $PM_{2.5}$ (2.5 $\mu g/m^3$).

The ARB relied on the Expert Elicitation process as the basis for concluding that hypothetical premature mortality may occur at $PM_{2.5}$ concentrations below the empirically-observed threshold of 7 $\mu g/m^3$, and may occur at or near ambient (background) concentrations of 2.5 $\mu g/m^3$. BNSF appreciates that ARB addressed the uncertainty in these estimates by calculating hypothetical premature mortality using both values to bound the $PM_{2.5}$ threshold concentration. Nonetheless, ARB did not address the practical implications of attributing hypothetical premature mortality to background levels of $PM_{2.5}$. If ARB's expert reviewers are correct, and $PM_{2.5}$ levels at or near 2.5 $\mu g/m^3$ contribute to hypothetical premature mortality, it introduces the possibility that even small additions to local $PM_{2.5}$ levels (e.g., from a new facility or a change in

activity of an existing facility), will yield increased estimates of death. We addressed the technical concerns regarding the extension of ARB's methodology to single or several nearby sources in Epidemiologic Concept Assumption 3. Our concern here is that the ARB's methodology is intentionally conservative for rulemaking purposes, and is particularly inappropriate for site-specific analyses. Further, we are concerned that findings of increased mortality for near-background levels of $PM_{2.5}$ attributable to local source(s) may effectively preclude industrial development and expansion. While it is appropriate for ARB to protect the health of Californians by establishing guidance on $PM_{2.5}$ concentration levels, in a heavily populated and industrialized state such as California, it is not practical to conclude that the economy can function without adding to ambient levels of $PM_{2.5}$. BNSF requests that ARB consider these implications and provide supporting guidance to address their practical implications.

Concluding Comments

In closing, BNSF believes that ARB is operating appropriately and within its mandate when the agency develops and provides analyses in support of future regulatory action. Further, we believe that it is in the best interest of ARB and of all Californians if the analyses are based on the best available science. However, neither industry nor the public is well served by the inappropriate application of scientific methods (e.g., use of the attributable fraction method to predict the number of hypothetical premature deaths prevented by achieving a specific decrease in $PM_{2.5}$ concentrations) or by using inherently imprecise methodology, developed from multiple assumptions and extrapolations, as in the methods used to estimate the contribution of DPM to $PM_{2.5}$ (please see our analysis in Appendix 1). BNSF requests that ARB seek alternative methods upon which to base regulatory impact analyses of DPM, and to conduct those analyses using assessment metrics that can be directly quantified.

BNSF appreciates the opportunity to provide comments to the ARB, and supports the process of ongoing scientific dialogue. We request that ARB consider our comments, and incorporate modifications based on our comments into the final report. We look forward to continued productive interactions with ARB, and are available to discuss these comments prior to finalization of the report.

Respectfully,

David C. Seep
Director Environmental Engineering and Program Development

cc: Dr. Rob Scofield, ENVIRON
Mr. Mark Stehly, BNSF

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Appendix 1.
Comments on Methodology Used to Estimate Ambient Concentrations of Particulate Matter from Diesel-fueled Engine Emissions

The Air Resources Board (ARB) draft report devotes considerable effort to the discussion and quantification of the effects in uncertainties in the concentration-response (C-R) function on the premature death estimates. Although uncertainties in the procedures used to model annual average diesel particulate matter (DPM) are discussed in Attachment 3, with a small paragraph also included in Section V (Uncertainties and Limitations), the quantification and discussion on their effect on the calculated premature deaths due to DPM exposure is not presented. When presenting such results, it is incumbent on the modeler to discuss and present the effects that uncertainties in the modeled DPM concentrations could have on the resultant risk estimates. The ARB reports falls short in this regard and presents the modeled DPM results with more certainty than they possess, thereby potentially misleading planners that may wish to use the report's results to make public policy. The following discussion illustrates some of the sources of uncertainty in the estimated (or modeled) DPM concentrations by using nitrogen oxide (NOx) concentrations as a surrogate. Based on these sources of uncertainty, an illustration of the potential effects on the resultant premature death risk estimates is presented.

The ARB report estimates the amount of DPM in California using the following equation:

$$S = \alpha C$$

Where,

S = Ambient DPM concentration estimates ($\mu g/m^3$)
C = Measured ambient NOx concentration ($\mu g/m^3$)
α = the DPM/NOx scale factor that is assumed to be 0.023 with a 0.006 standard deviation

The scale factor α was estimated by analyzing Chemical Mass Balance (CMB) source apportionment (SA) modeling results from several studies:

- Children's Health Study (CHS, 2000) that performed CMB receptor modeling for 11 sites in the South Coast Air Basin (SoCAB) region of Southern California;

- Central Regional Particulate Air Quality Study (CRPAQS, 2000) that performed CMB modeling for 6 sites in Central California; and

- Diesel-Gasoline Particulate Split Study (DGPSS) for two sites in Southern California.

Some of the findings of these studies were:

PM source apportionment depends on the measurement technology used and in particular, the carbon particulate measurements (elemental carbon/organic carbon)

where different DPM apportionment was found using the IMPROVE (California Regional PM10/PM2.5 Air Quality Study [CRPAQS]) versus National Institute for Occupational Safety and Health (NIOSH) [CHS]) Carbon measurement techniques;

1. Areas of high NOx or DPM concentrations skew the influence of the source apportionment factor;

2. The large variability in the DPM/NOx ratio illustrated by the large standard deviation leads to large uncertainty;

3. The SA is very sensitive to the choice of source profiles used; and

4. A substantial source of uncertainty is related to the off-road diesel contribution as diesel profiles are primarily based on measurements from on-road diesel mobile sources.

Additionally, for the DGPSS, two separate researchers (Schauer and Fujita) performed measurements and CMB modeling at co-located monitoring sites and time periods and derived DPM/NOx scale factors that varied by a factor of two, $\alpha = 0.010$ (Schauer) versus 0.023 (Fujita) when using the different carbon measurement technologies and their own CMB modeling techniques.

The CHS found scale factors that averaged 0.024, whereas CRPAQS found a value of 0.017. The ARB report lists numerous iterations of scale factors derived from the CMB modeling, with the final numbers as follows:

Study	**Scale Factor α**	**Standard Deviation**
CHS	0.024	0.011
CRPAQS	0.017	0.009
DGPSS-Schauer	0.010	0.003
DGPSS-Fujita	0.023	0.004

The ARB report also notes that another technique for estimating the scale factor used by LLNL and ARB's MLD estimated scale factors that agree with the DGPSS-Schauer value ($\alpha = 0.010$). We note that CMB modeling performed by the South Coast Air Management District (SCAQMD) for the Multiple Air Toxics Exposure Study (MATES-III) estimated scale factors that are closer to the DGPSS-Fujita value ($\alpha = 0.023$).

The ARB report then compares the SA DPM scale factor modeling results with ratios derived from emission inventories (EIs) whose estimates they note "may be visualized as tons of pollutants emitted each day into a well mixed box covering each county, with removal rates of DPM and NOx proportionately the same." The ARB report then derives a scale factor of 0.023 (standard deviation of 0.006) using the EI ratio method.

The above discussions are contained in Attachment 3 of the ARB report. In the body of the ARB report (Section F.), the discussions on the uncertainties in the DPM/NOx scale

factor are not presented and instead the agreements between the SA and EI approaches for deriving the α = 0.023 scale factor is emphasized. This approach implies a sense of certainty in the estimate and is used to justify the selection of a single value that is applied to annual average NOx measurements to obtain DPM concentrations for the entire state of California. However, it is important to note that for many of the more rural locations there are no NOx measurements. To address this fact, the ARB report quotes an internal analysis that reportedly derived a relationship between NOx concentrations and measured particulate nitrate (NO_3) concentrations which found ranges of 30% to 50% (Motallebi, 2006). ARB selected a value from the mid-point of this range ([NOx] = 0.4 [NO_3NH_4]) to convert NO_3 to NOx concentrations at IMPROVE monitoring sites that tend to be located in more remote/rural Class I areas.

Discussion of DPM Modeling Methodology

As noted above, there are numerous uncertainties associated with the modeling of DPM concentrations. However these uncertainties are not quantified or discussed in the interpretation of the health modeling results. The use of NOx concentrations as a surrogate for DPM is highly questionable given that NOx is emitted from all combustion sources, not just diesel, and such sources are not uniform across California. Furthermore, the representativeness of the ~114 NOx monitoring sites for characterizing all of California is also highly suspect. This is pointed out by the Peer Reviewers who note that DPM exposure may be higher than indicated in close proximity to DPM source complex regions. However, the Peer Reviews did not acknowledge the fact that many of the NOx monitors are sited to evaluate compliance with the annual NO_2 standard so are situated in locations to measure maximum NOx concentrations, not regionally representative average concentrations.

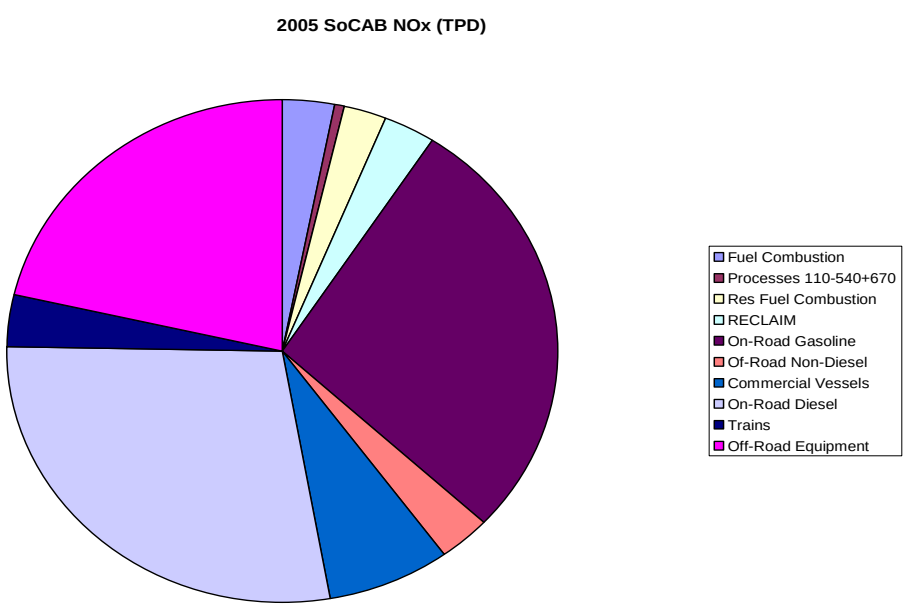

Figure 1. Distribution of NOx emissions across major source categories in the SoCAB (Source: Appendix A-2 from http://www.aqmd.gov/aqmp/07aqmp/aqmp/Appendix_III.pdf).

The latest 2007 Air Quality Management Plan (AQMP) for the SoCAB for 2005 (Appendix A-2 from http://www.aqmd.gov/aqmp/07aqmp/aqmp/Appendix_III.pdf) provides a breakdown of NOx emissions by source category. As illustrated by Figure 1, the distribution of NOx emissions by source categories in the SoCAB show that diesel engines are only a little over half (53%) of the NOx emissions (this assumes all off-road equipment NOx is from diesel). Of the diesel DPM emissions in the SoCAB, half (50%) are from off-road equipment; the ARB report notes that off-road equipment represents a significant source of uncertainty a considerable source of uncertainty in the CMB SA modeling of DPM (page A-14). Based on the MATES-III modeling database (Figure 2), it is expected that off-road diesel represents the majority of DPM emissions. The distribution of the diesel NOx sources (e.g., trains, off-road equipment, HDDTs, etc.) emissions, and consequently DPM emissions, will be different than much of the non-diesel NOx sources (e.g., REgional CLean Air Incentives Market (RECLAIM) point sources, residential heating, on-road mobile sources, etc.). Consequently, assuming a single uniform 0.023 scaling factor across the SoCAB introduces uncertainty in the analysis that is difficult, but not impossible, to quantify.

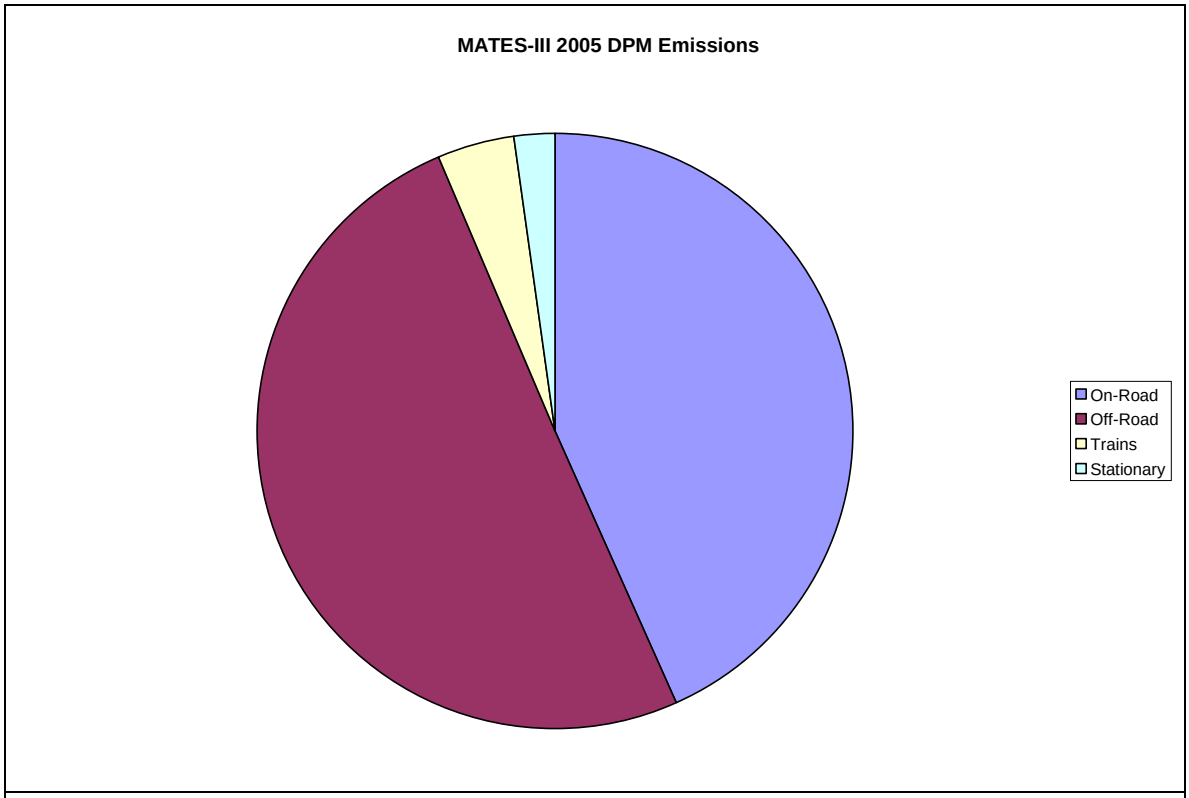

Figure 2. Distribution of DPM emissions across major source categories in the SoCAB (Source: MATES-III Appendix IV).

The analysis of CMB SA modeling developed four average values for the α scale factor based on the CHS (0.024), CRPAQS (0.017), DGPSS-Schauer (0.010) and DGPSS-Fujita (0.023) studies. The DGPSS-Schauer scale factor was supported by analysis by LLNL and ARB MLD (0.010), and the DGPSS-Fujita scale factor was supported by MATES-III (0.023). The 0.023 scale factor was selected because it was also supported by an emission inventory (EI) DPM to NOx ratio analysis of county-level emissions.

However, the EI ratio analysis is based on the major assumption that the “removal rates of DPM and NOx are proportionately the same” (page A-18). However, this is not a valid assumption as DPM is inert particulate matter that exists primarily in the fine ($PM_{2.5}$) mode, whereas NOx is a highly reactive gaseous species. The primary removal mechanism for DPM will be wet and dry deposition, whereas the primary removal mechanism for NOx will be chemical reactions. Warnek (2000) and Jaenicke (1982) estimate residence times of $PM_{2.5}$ of approximately 5 days; in Southern California where precipitation is scarce, residence times may be longer. This is confirmed by Seinfeld and Pandis (1998) who note that the “residence time of particles in the troposphere vary only from a few days to a few weeks” (p. 98). However, for NOx Seinfeld and Pandis (1998) state that “From a number of observational studies, it has been estimated that the characteristic time for conversion of NOx to other NOy (i.e., chemical species that contain the elements N and O but are not NOx) species is 4 to 20 hours" (p. 72). The residence time of NOx in the polluted Southern California atmosphere would be less. Given these differences in atmospheric lifetimes between NOx and DPM, we would not expect an EI-derived and an atmospheric concentration-based DPM/NOx ratio to be the same. Thus, when both approaches apparently yield a 0.023 scale factor, it suggests a potential error rather than a corroboration of methods.

The use of a single scale factor also introduces uncertainty in the analysis. Figure 3 displays the spatial distribution of the DPM/NOx emissions ratios in the SoCAB for a March weekday from the MATES-III modeling database (http://www.aqmd.gov/prdas/matesIII/matesIII.html). The EI based scale factors range from 0.004 to 0.100 across the SoCAB. Thus, the EI DPM/NOx emissions ratio analysis support use of both the 0.010 and 0.023 DGPSS-derived scale factors, which provides a quantitative range of uncertainty in the modeled DPM estimates.

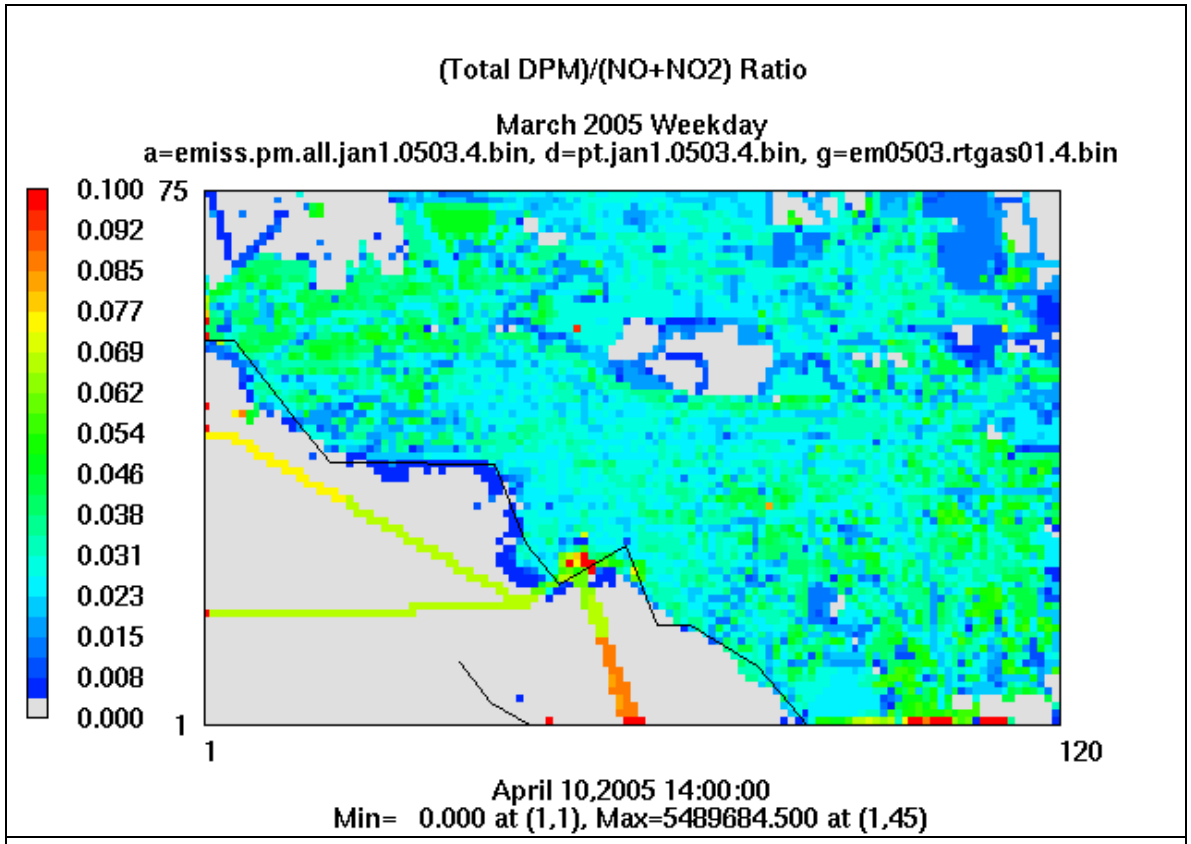

Figure 3. Spatial distribution of DPM/NOx emissions ratios in the SoCAB from the MATES-III modeling database.

The effects of using IMPROVE particulate NO_3 measurements to derive NOx concentrations using data analysis results from Motallebi (2006) on the DPM modeling uncertainty could not be analyzed because the internal ARB report is not readily available. As stated in the ARB report, Motallebi (2006) reported NOx concentrations that ranged from 30% to 50% of the measured ammonium nitrate concentrations, which if true provides some uncertainty bounds. However, given that these measurements occur in more rural areas their effects on the calculated risk are likely very small.

Summary of DPM Modeling Uncertainties

The procedures used to estimate DPM in the ARB report has numerous assumptions and uncertainties:

- DPM concentration estimates can be derived from NOx concentrations using a 0.023 scale factor across California: The ARB discussion of CMB SA studies found several scale factors that ranged form 0.010 to 0.024.

- The CMB provides an accurate estimate of the DPM/NOx scale factor: The CMB derived scale factors are highly uncertain and possess numerous levels of uncertainty that needs to be quantified in the risk calculations:

- They are highly dependant on the DPM source profile selected that is representative of on-road mobile diesel vehicles.
- The off-road diesel equipment is not well characterized by the CMB modeling, at least for the SoCAB such sources represent half of the DPM emissions in the SoCAB.

- The EI-derived scale factor of 0.023 is based on the assumption that DPM and NOx have the same removal rates and spatial variation, which supports its use in the DPM modeling: As NOx has much faster removal processes than DPM, this analysis is based on an erroneous assumption. Furthermore, at least for the SoCAB, the spatial variation in the DPM/NOx emission ratios range from 0.004 to 0.100 so support all of the SA-derived scale factors (from 0.010 to 0.024).

- The NOx monitoring network fails to adequate represent the spatial variation in DPM concentrations: The NOx monitoring network fails to capture all of the high density DPM source locations so would understate the DPM concentrations in those locations. Many of the NOx monitors were sited for compliance determination of the NO_2 standard so are designed to capture maximum concentrations and would overstate regional average NOx concentrations.

The ARB report notes that "the source apportionment studies are considered the best available methods for determining ambient DPM concentrations" (p. A-14). Regarding the differences between the DGPSS-Schauer (0.010) and DGPSS-Fujita (0.023) scale factors, the ARB report states that "Without a priori information about which method is more accurate, we believe both estimates should be weighted equally, giving DPM/NOx =0.065 (0.009)." The ARB report then contradicts itself by relying on the high end scale factor (0.023) based on a questionable EI analysis, that as discussed above, has numerous uncertainties.

Section III.D of the ARB report presents the results of the premature deaths associated with exposure to DPM. Results are presented using the 0.023 scale factor and the central estimate of the relative risk in premature death (10 percent per 10 $\mu g/m^3$ increase in $PM_{2.5}$), as well as a low and high relative risk estimates (3 and 20 percent increase per 10 $\mu g/m^3$ increase in $PM_{2.5}$). These results from the ARB report for the DPM premature deaths are presented in the first row in Table 1 below. The second row follows the ARB methodology, only using the 0.010 scale factor, which as noted in Appendix 3 of the ARB report makes an equally valid argument as was made for the 0.023 scale factor (presented in the second row in Table 1). The third and fourth rows use the 0.023 and 0.010 Scale Factors, but adds in uncertainties associated with the DPM modeling approach, for which the range in Scale Factors of 0.004 and 0.100 are used based on the range of EI-based scale factors across the SoCAB in absence of better estimates. The ARB Report methodology estimates approximately 4,000 premature deaths due to DPM exposure in California with an uncertainty range that spans a factor of ~6 from 1,200 to 7,100. Using what appears to be an equally valid 0.010 Scale Factor results in an average of 1,700 premature deaths due to DPM exposure and uncertainties that also span a factor of 6 from 520 to 3,100. Accounting for the uncertainties in the DPM modeling doesn't affect the mean values (3,900 and 1,700 premature deaths using the 0.023 and 0.010 Scale Factors) but the uncertainties

in the estimates are much larger spanning a factor of 150, from 210 to 30,900 premature deaths, which probably provides a much more realistic estimate of the uncertainties in the calculations.

Table 1. Comparison of premature death estimates due to DPM exposure in California using the ARB Report methodology accounting for uncertainties in the risk factors and using alternative Scale Factor and accounting for uncertainties in DPM modeling.

Scenario	**Low**	**Mean**	**High**
ARB Report (0.023 Scale Factor), uncertainties in risk factor	1,200	3,900	7,100
Use of 0.010 Scale Factor, uncertainties in risk factor	520	1,700	3,100
0.023 Scale Factor, uncertainties in DPM modeling	210	3,900	30,900
0.010 Scale Factor, uncertainties in DPM modeling	210	1,700	30,900

References cited in Appendix

CHS (1995) as cited in ARB Appendix 3. Manchester, J., Schauer, J., and Cass, G. Determination of the Elemental Carbon, Organic Compounds and Source Contributions to Atmospheric Particles During the Southern California Children's Health Study: Part B: The Distribution of Particle-Phase Organic Compounds in the Atmosphere and Source Contributions to Atmospheric Particulate Matter Concentrations during the Southern California Childrens' Health Study, 1995. Final Report for the California Air Resources Board.

California Regional PM10/PM2.5 Air Quality Study (CRPAQS, 2005) as cited in ARB Appendix 3. Chow, J., Chen, L.W., Lowenthal, D., Doraiswamy, P., Park, K., Kohl, S., Trimble, D., and Watson, J. California Regional PM10/PM2.5 Air Quality Study (CRPAQS): Initial Data Anaysis of Field Program Measurements, Final Report, 2005 for the California Air Resources Board.

Diesel-Gasoline Particulate Split Study as cited in ARB Appendix 3. The DOE Gasoline/Diesel PM Split Study, Presentations by D. Lawson, E. Fujita, and J Schauer, California Air Resources Board Seminars webpage: and DOE/NREL Gasoline/Diesel Split Study webpage.

Seinfeld, J.H. and S.N. Pandis. 1998. Atmospheric Chemistry and Physics. John Wiley & Sons, Inc. ISBN 0-471-17815-2.

Warnek, P. Chemistry of the Natural Atmosphere. Academic Press. ISBN No. 0-12-735632-0.

Note that ARB Appendix 3 does not provide references for LLNL (2007; Motabelli (2006) or ARB MLD (2003).

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Via email submission:
Re: Health Impacts Analysis: PM Premature Death Relationship May 22, 2008 Draft

July 11, 2008

Dear Dr. Tran,

On behalf of its members, which are leading manufacturers of diesel engines and diesel-powered vehicles, refiners of diesel fuel, and producers of emission control equipment, the Diesel Technology Forum offers these comments on the staff draft report titled "Actions to Update the Methodology for Estimating Premature Death Associated with Fine Airborne Particulate (PM2.5) Exposure".

As you know, considerable changes have taken place in diesel fuels, engines and after-treatment technology since the original adoption of the 2000 CARB Toxic Air Contaminant designation and subsequent risk reduction requirements. For example, a new 2008 generation highway diesel truck has 1/60th the level of soot emissions compared to a truck manufactured in 1988. Both the advent of new emissions control technology as well as the considerable modernizing and upgrading of the existing vehicle and equipment fleet, have led to a substantial improvement in the overall contribution of diesel engines to California's air quality inventory for which we present detailed information and a research report below.

We believe it is imperative that any future risk, regulation, or other decisions are based on the most recent emissions inventory and risk data, particularly with regard to lower levels of diesel emissions in California's air. More specific comments are as follows:

1. Adoption of the staff draft should be postponed pending further scientific review of recent California-specific data concerning prevalence and severity of PM-related health effects.
A panel of well-qualified academicians has recently petitioned for review of CARB's earlier determination that the particulate matter (PM) component of diesel exhaust is a toxic air contaminant. We share their concern that the initial determination, now ten

years old, and the proposed revision *upward* of the risk of premature deathwhich can be attributed to PM, are based on outdated, unspecific and incomplete information.

2. **Levels of Diesel PM in CARB Emissions inventory have been steadily declining due to new cleaner fuels and technology; inconsistent with proposals to increase risk attributable to diesel exhaust.**
Declining statewide PM emission levels are at apparent variance with the sharply *downward* trend of diesel emissions in California, attributable to clean diesel technology and the development of ultra low-sulfur diesel fuel. According to the draft staff report, in fact, since 1999, annual average PM 2.5 levels have *decreased* 30% statewide, the statewide average PM concentration has *declined* to new low levels, and PM 2.5 exposures are much *reduced* from earlier levels.

Research sponsored by the Diesel Technology Forum and conducted by Sierra research substantiates this trend in PM emissions. Our research reviewed the emissions inventory data from CARB taking in consideration all adopted diesel -- related regulations and their published benefits, and found that brake and tire wear will be the primary sources of fine particles in Southern California air as early as next year, with diesel PM falling to a less significant level of the overall statewide inventory. We incorporate by reference and submit this report SR2005-02-01 “The Contribution of Diesel Engines to Emissions of ROG, NOx, and PM2.5 in California: Past, Present and Future” with these comments and encourage its review and incorporation into your decision-making process.

Continuing uncertainty about the factual basis for CARB’s regulatory action casts doubt on the cost-effectiveness of its actions, at least subsequent to the TAC designation in 1998. Despite the continuous improvement in levels of PM emissions noted above, and substantial advances in clean diesel technology, it is estimated that the private sector has so far been required to bear TAC-related costs of morethan $10 billion. The proposed increase in rate of health risk associated with exposure to PM 2.5 has been prepared by CARB staff in connection with CARB’s “Goods Movement Emission Reduction Plan for Ports”. The incremental costs of that program, justified in part by the staff assessment of exposures to PM 2.5, are estimated by Dr. Miller to be $8 billion, in addition to $1 billion of Proposition 1B public funds.

Of course, the costs of these programs, however high, should not be the only measure of their efficacy. Californians deserve both clean air and of a full, accurate accounting of costs which are attributable to environmental regulation. Given the large sums at stake, it is appropriate to examine whether programs such as GMERP are cost effective, and whether their laudable public health and environmental goals can be best achieved through these or other means. As our research highlights, the overall levels of diesel PM are projected to decline consistently over time. While a specific contribution of diesel exhaust to PM risk overall has yet to be determined, the diesel industry readily acknowledges its obligation to meet all relevant regulatory requirements, and is fully committed tothe continuous improvement of its environmental performance. The dramatic reductions in levels of diesel PM emissions and exposures over the last decade demonstrate that, working together industry and government can achieve remarkable progress.

Because of limits on the availability of public and private resources for these purposes, it behooves us to make optimal use of those which can be brought to bear is solving truly urgent environmental problems. It is for this reason that we encourage you to follow the scientists' recommendation of due caution in adopting the staff proposal and to carefully consider our emissions inventory analysis submitted with these comments. It is imperative that new regulations be fully informed by current, California-specific data and by acknowledgement of the progress which has so far resulted in reduction of diesel exhaust emissions by more than 90%.

Allen R. Schaeffer

Allen R. Schaeffer Executive Director

Attached: Sierra Research Report SR2005-02-01: "The Contribution of Diesel Engines to Emissions of ROG, NOx, and PM2.5 in California: Past, Present and Future

Warner North, NorthWorks, Inc., Belmont CA

Comments on the California Air Resources Board (CARB) Draft Staff Report, *Methodology for Estimating Premature Deaths Associated with Long-term Exposure to Airborne Fine Particulate Matter in California*, and Presentation, both dated May 22, 2008

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Disclaimer

Both my comments at the workshop on June 25, 2008, and these written comments expanding on what I said in the brief time allotted to me at the workshop, are under the sponsorship of Western States Petroleum Association (WSPA). This organization is paying for my time in preparing these comments and my travel expenses. The content of the comments is entirely of my own choosing. These comments should not be taken as representing the views of the WSPA or any of its member companies.

My Background and Experience

My expertise is in decision analysis and expert elicitation. I have my Ph.D. from Stanford University, and I have been on the Stanford faculty since 1976; I am now a consulting professor in the Department of Management Science and Engineering. My main employment since 1967 has been with a series of consulting firms: SRI International (Menlo Park, CA), Decision Focus Inc.(Mountain View, CA, no longer in business), and, for the past ten years, NorthWorks, Incorporated (Belmont, CA).

I have served on the California Governor's Scientific Advisory Panel for Proposition 65 (1987-89) and the Independent Science Board of the California Bay Delta Authority (2005).

I have participated in numerous committees, panels, and boards of the National Research Council (NRC) of the National Academies (National Academy of Sciences, National Academy of Engineering, The Institute of Medicine). I am a National Associate of the National Research Council, which means I can use the Members' Library behind the Einstein statue on Constitution Avenue.

I am a past president of the Society for Risk Analysis and a recipient of its "Outstanding Risk Practitioner" Award. I have been on the editorial board for its journal, *Risk Analysis*, for several decades. Since April of this year, I am the area editor for

decision sciences for this journal.

I am a past recipient of the Ramsey Prize for lifetime achievement from the Decision Analysis Society.

I have served on committees of the United States Environmental Protection Agency (EPA) Science Advisory Board (SAB), beginning in 1978 on a subcommittee of the SAB set up to provide advice on expert elicitation in the form of probabilities, on the health effects of ambient ozone. I served as a peer reviewer for the draft report from EPA on the PM expert elicitation process dated August, 2006. I also served as a peer reviewer for the earlier "pilot" version of this process.

Other details of my past experience and background are available at my website (www.northworks.net) or from my CV, available on request.

Main Message:
My Review of EPA's Expert Elicitation on Fine Particulate Matter Does Not Endorse Use of the Resulting Numbers for Regulatory Decision Making

I quote from page 8 of my peer review for EPA dated September 25, 2006, of the "Expanded Expert Judgment Assessment of the Concentration-Response Relationship between $PM_{2.5}$ Exposure and Mortality" Draft Report dated August 25, 2006:

> I would not want to see EPA take this report into a federal courtroom and cite it as a principal basis for the EPA Administrator's decision in setting a NAAQS standard for $PM_{2.5}$.

I urge the State of California similarly: The State should not view this EPA report as more than a commendable initial effort to assess judgment, from 12 experts selected by EPA staff and contractor, in the form of probability distributions on mortality resulting from low-level exposure to ambient fine particulate matter. It should not be a principal basis for regulatory decision making on $PM_{2.5}$ for the California Air Resources Board and the California State Government.

Discussion on CARB Draft Staff Report and Presentation

There is much I like in the CARB Methodology Draft Staff Report of May 22, 2008 and the ARB presentation of May 22, 2008:

• CARB's emphasis on PM especially fine PM ($PM_{2.5}$) as an important threat to human health, including premature mortality and morbidity. The available epidemiological evidence is persuasive that some PM mixtures at high ambient levels cause premature mortality and morbidity. In my judgment, fine PM is perhaps the most important ambient air pollutant for its human health impacts.

• Disclosure of wide range of uncertainty in mortality estimates, including on the first page of the Executive Summary and pages 10, 17, 18 of the presentation

• Identification of diesel engine emissions as an important source of fine

particulate emissions

• Disclosure that differences in size and chemical composition may be important determinates of health impacts from fine particulate exposures, and that more research is needed to determine which PM sources are most dangerous. (However, such disclosure is not in the presentation, and it is hard to find in the Draft Staff Report. On bottom of page 21 the disclosure is stated in the negative as “not adequate evidence at present ... to make any formal adjustments”.)

• Maps showing how particulate levels in California have decreased substantially over time. (Page 13 of the presentation). I find this progress encouraging.

But there is also CARB material that I think is in need of improvement and refinement.

• Single-number estimates on premature deaths from emissions (CARB Press releases of June 10, 2008: “Air Board Proposes world’s strictest regulation curbing emissions from ocean-going vessels;” ARB Press release of May 12: “ARB proposes new rules to clean up state trucks, buses. Presentation, Regulation for Drayage Trucks;” Board Hearing, December 7, 2007: page 12,13,30,31. These single-number estimates stated with two significant digits suggest a precision in our scientific understanding that simply is not there.

• There is not sufficient emphasis on the need for further research to determine which PM sources are most dangerous.

• Citation of EPA “Expert Judgment Assessment” report as firm support for setting PM regulation in California. I was a peer reviewer for this report. I object, especially to the summary wording in the CARB Draft Staff Report on page 20, especially to the last sentence of section B. As one of the reviewers listed, I most emphatically do not “agree” as stated in this sentence.

• CARB should follow the U.S. EPA in basing regulatory decisions on the overall scientific information, with appropriate consideration of uncertainty including scientific judgment. Formal probabilistic analysis including model uncertainty in risk assessment was not carried out for the 2007 proposed revision of the ozone national ambient air quality standards (NAAQS). Application of formal uncertainty methods to fine particulate matter is even more complex than application of these methods to ozone. CARB should consider carefully three documents: The Rochester Report (a copy of which I provided on June 25 to Linda Smith; additional copies available on request); EPA’s *Responses to Significant Comments on the 2007 Proposed Rule on the National Ambient Air Quality Standards for Ozone* (March 2008), and a 2007 review article by Roger McClellan, Suresh Moolgavkar (two of the authors of the Rochester Report) and colleagues, “Evidence of Health Impacts of Sulfate- and Nitrate-Containing particles in Ambient Air,” *Inhalation Toxicology*, 19:419-449, 2007.

• CARB has emphasized regulation of diesel engines. It should also emphasize regulation of other major sources of airborne fine particulate matter, such as smoke from forest fires.

Discussion of These Five Points on Which Improvement and Refinement Is Needed

Lack of Explicit Statement on Uncertainty in Mortality Estimates: The CARB press releases are not consistent with communication in the CARB May 22 Draft Staff Report and presentation. I urge CARB press release practice be corrected to indicate the wide range of uncertainty in estimates of premature mortality, cancer cases, and morbidity.

Importance of Chemical Composition and Other Differences among fine particulate mixtures. The development of a systematic program to assess the toxicity of different components of the particulate matter mixture is very important for California, for the United States, and for the world. Reference: See National Research Council, 2004: *Research Priorities for Airborne Particulate Matter*, Vol. 4, pp 8-9, and 130-132.

> Here is a short quotation from this report to compare with the wording in the CARB Draft Staff Report on the bottom of page 21:
>
> The current NAAQS for PM is both size and mass-based and implicitly assumes that all particles of a given size have the same toxicity per unit mass, irrespective of chemical composition. In the committee's judgment, this mass-based NAAQS greatly oversimplifies complex biological phenomena. … A better understanding of characteristics that modulate toxicity could lead to targeted control strategies specifically addressing those sources having the most significant adverse effects on human health. (p. 8)

I was one of the peer reviewers of this 2004 NRC report, along with Morton Lippman and C. Arden Pope. The authoring committee was chaired by Jonathan Samet and included Roger McClellan, Mark Utell, Daniel Krewski, and other leaders in the scientific community on the health effects of airborne particulate matter.

The 2007 article by Roger McClellan, Suresh Moolgavkar, and colleagues looks reviews evidence on health impacts of sulfate- and nitrate-containing particles, noting the complexity of the data and judgments involved. The article urges caution, especially in attributing a causal relationship for health impacts. Several commenters (James E. Enstrom, M.D., Dr. John Heiss) at the June 25 workshop, who have extensive expertise in epidemiology, similarly expressed the need for caution in interpreting epidemiological results for fine particulate matter, and urged more emphasis on results from California studies showing a lower level of health impacts. The EPA Expert Judgment Assessment exercise asked for judgment on premature mortality from exposure to fine particulate matter ($PM_{2.5}$) measured solely on a mass basis, without considering variation based on sources and chemical composition. CARB needs to use a more sophisticated and comprehensive assessment of the scientific information than simply using numbers taken from this EPA exercise.

The EPA Expert Judgment Assessment Exercise of 2006. I shall begin by summarizing the history of EPA's use of the expert elicitation methodology. I shall make extensive use of the book by M. Granger Morgan and Max Henrion, *Uncertainty:*

A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis, Cambridge University Press, 1990, especially chapters 6 and 7. (This book is cited on page 23 of the ARB Draft Staff Report. The senior author, Granger Morgan, is currently the chair of the Executive Committee of EPA's Science Advisory Board.)

SRI International, and in particular its Decision Analysis Group, for which I was then assistant director, gave a seminar to EPA Air Office staff on assessment of expert judgment in the form of probabilities. The methods are described in Morgan and Henrion, pages 141-146. These methods were then used on ozone by the EPA Office of Air Quality Planning and Standards (OAQPS). There was SAB review by a subcommittee including Granger Morgan and myself, beginning in 1978. The review recommended that EPA should carry out further research and development before attempting to use these methods in support of regulatory decision making. Following a research exercise on carbon monoxide, EPA then carried out an application to ambient lead, described in Morgan and Henrion, page 154-156, in the mid-1980s. Two decades then passed without additional use of these methods by OAQPS.

After John Graham (a Ph.D. student of Granger Morgan's and an advocate of such methods) became the Director of the Office of Information and Regulatory Affairs (OIRA) within the Office of Management and Budget (OMB), EPA OAQPS again took an interest in the application of expert elicitation methods to diesel emissions and fine particulate matter. EPA's interest in improved methods for characterizing uncertainty on the health effects of air pollutants was encouraged by the 2002 National Research Council report (cited on page 10 of the Draft Staff Report). EPA first did a "pilot" exercise with 5 experts, and then a larger exercise using 12 experts. EPA is currently carrying out, through its Science Advisory Board and Advisory Council on Clean Air Compliance Analysis, reviews on how to do and interpret the expert elicitation. (See the EPA SAB webpage:
http://yosemite.epa.gov/sab/sabproduct.nsf/f697818d4467059f8525724100810c37/e13622b0f6b18d8f8525727b006ffb3b!OpenDocument and Minutes of the meeting on May 8, 2008:
http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/ABC3904D8E9E512E852573FA006014AC/$File/COUNCIL+5-8-08+Minutes+PM-EE.pdf .)

I shall use three quotes from Morgan and Henrion, 1990, end of Chapter 7, page 169, as motivating the need for caution in applying these expert elicitation methods:

> Because the results of full probabilistic analyses using elicited subjective expert judgment can easily get complicated, there is a strong temptation in some policy analytic contexts to use these techniques to produce "snow jobs."
>
> …
>
> Failure to exercise appropriate norms of quality control could lead to the techniques acquiring a bad name in some circles and could significantly impede their wider adoption.
>
> …
>
> Just as good outdoorsmen don't leave trash behind on the trail, good analysts should try not to leave alienated experts behind on their trail.

I assert Dr. Roger McClellan is Exhibit A as an "alienated expert." Dr. McClellan is a former chair of CASAC, a past president of the Society for Toxicology, with decades of experience in research on the health impacts of air pollution. He testified on July 19, 2006 to the Senate Environment and Public Works Committee http://epw.senate.gov/public/index.cfm?FuseAction=Hearings.Testimony&Hearing_ID=cf926186-802a-23ad-4317-dc5625ad2073&Witness_ID=6ccc00dd-aa9a-4e8e-bd97-b3f7a39ebb32.

I quote from Roger McClellan's testimony:

> "Expert elicitations of opinion on PM2.5 risks are very likely flawed with a blurring of the distinction between scientific evaluation and policy choices." (final summary point, page 1)
>
> "I served as one of the five experts in EPA's pilot project to elicit opinions on the relationship between $PM_{2.5}$ exposure and death." (page 11)
> …
> In the session I participated in, I found the interviewer focusing on eliciting quantitative linear exposure-response coefficients. Since it is my professional opinion that it is very unlikely that a linear relationship exists between $PM_{2.5}$ exposure and health responses down to and including current ambient levels, the interview and the follow-up discussions proved frustrating for both me and the interviewer. (page 11)
> …
> I have serious reservations as to its [expert elicitation] use in eliciting *quantitative* characterizations of risk for various levels of $PM_{2.5}$ exposure for different populations in different parts of the United States. (page 11)
> …
> I am also concerned about the process used to select experts for participation. (page 12)
> …
> I would urge the Administrator to not use the results of the expert opinion elicitation as input for quantitative estimates of the risks/benefits associated with $PM_{2.5}$ exposure. Such an approach is not a substitute for more rigorous uncertainty analysis that attempts to characterize all the factors that impact on estimating risks of $PM_{2.5}$ exposure and the benefits of reductions in the $PM_{2.5}$ exposure. (page 12).
>
> I quote from Morgan and Henrion, 1990, page 156-157, regarding the mid-1980s EPA expert elicitation exercise:
>
> In several EPA/CASAC meetings, Warner North has argued that although excellent, the Wallsten/Whitfield protocol [used by EPA for expert elicitation on lead in ambient air – see p. 154-156] does not place as much emphasis as it might on getting experts to articulate their reasons for the judgments they make, or on documenting these reasons. North has argued that such argumentation is important if the full benefits of elicitation are to be available to the standard setting process, and he has urged that more attention be directed at developing

such material in future EPA-sponsored elicitations.

I made a similar point in my 10 pages of reviewer comments in the EPA Expert Judgment Assessment exercise on fine particulate matter in 2006:

> … I would like to be sure I am on record as urging resistance to the temptation toward making specific decisions based on this type of cost-risk-benefit numerology without shared understanding of what the numbers represent.
> (Page 9, under "strengths and weaknesses")

The $PM_{2.5}$ Expert Judgment Assessment exercise was the next time - twenty two years after the lead application - that expert elicitation was done at EPA (at least in the context of health impacts of ambient air pollutants). My review emphasized the positive potential of the methodology and praised the contractors for their work. I urge that CARB read the comments from me and the other peer reviewers, rather than the summary of our comments prepared by EPA or its contractor, which I never reviewed or endorsed. (The final version of this EPA report, including my comments as submitted, is available at: http://www.epa.gov/ttn/ecas/regdata/Uncertainty/pm_ee_peer_review_summary.pdf.)

I emphasized in my review that I thought EPA's contractor (Katherine Walker, assisted by Patrick Kinney, working through Industrial Economics, Incorporated), had done a good job, particularly in documenting what was done, what was not done, and summarizing the discussion with each expert. I raised questions about the expert selection process and the 12 experts chosen. I never endorsed this EPA exercise as adequate as a basis for standard setting or regulatory decision making. My comments endorsed it as a useful beginning, for discussion within the scientific community on how to characterize uncertainty better, as urged in the 2002 NRC report. In my review for EPA I urged that such discussion be encouraged. I am pleased such discussions are now underway through EPA's Science Advisory Board. I urge such discussions through CARB at workshops such as the workshop held on June 25. (But I observe that there was no opportunity for discussion among the commenters and just five minutes allotted to each person who wished to comment. In my experience, this meeting was not a "workshop," but a meeting to solicit public comments.)

Other Review and Discussion on EPA Risk Assessment Methodology

I participated in a workshop last June at the University of Rochester organized by Mark Utell, a health expert, a long-time member of CASAC, and one of the 12 experts in the 2006 EPA Expert Judgment Assessment exercise. This workshop addressed EPA's risk assessment for ozone, which supported EPA's recent revision of the NAAQS for ozone. Roger McClellan chaired our panel of ten experts. Our report is available and was submitted to EPA as a part of the comment process on the revision of the NAAQS for ozone. A slightly reorganized version has been submitted for publication in the *Journal of Air and Waste Management*. Much of the funding for the University of Rochester workshop came from the petroleum industry, through the American Petroleum Institute. API had no influence over the content of the workshop and the ensuing report. An observer from EPA (Harvey Richmond) attended the workshop and

answered questions about EPA's risk assessment process. As noted in the EPA *Responses* document (on page 79) discussed below, Harvey Richmond is the person to go to at EPA for all the files and technical support documents for the EPA health risk assessment. He has been associated with risk assessment for criteria air pollutants at EPA for at least 30 years, back to the work I reviewed as part of the SAB in 1978. I believe he was one of those from EPA in North Carolina on the telephone June 25.

The report resulting from the University of Rochester workshop is discussed as the "Rochester Report" in EPA's *Responses to Significant Comments on the 2007 Proposed Rule on the National Ambient Air Quality Standards for Ozone*: http://www.epa.gov/ttnnaaqs/standards/ozone/data/2008_03_rtc.pdf, beginning on page 5. In this document the EPA states repeatedly that its proposed regulatory decision in revising the ozone NAAQS was a judgment call based primarily on new clinical studies, and not the quantitative risk assessment, and that its risk assessment methodology and results were carefully reviewed by CASAC in public meetings. The "Rochester Report" points out limitations in EPA's risk assessment, and EPA does not disagree. For example, in *Responses* on page 81: "Another comment (The Rochester Report) asserted that EPA ignored model uncertainty in its health risk assessment." On page 82 EPA responds as follows: "With respect to choice of models to rely upon in the risk assessment, EPA agrees that recent work on model sensitivity has raised new concerns and that the agency has given much attention to this issue." EPA notes a comment (#13, page 86) from the Rochester Report (and others) that EPA should conduct an "integrated uncertainty analysis" such as called for in the 2002 National Research Council report. EPA responds as follows: "While the Agency is currently developing these approaches, such comprehensive assessments of uncertainty are not available for the current O3 risk assessment for this NAAQS review." (*Responses*, page 97).

EPA in the *Responses* document cites several instances in which the "Rochester Report" appears consistent with its Proposed Rule:

1. "The EPA generally agrees with the Rochester Report's evaluation of the Adams (2006) study and the interpretation of the EPA' secondary analysis of the data." See *Responses*, pages 23-24, with quotation from Rochester Report, pages 56-57.

2. *Responses*, page 57: "Further, the Rochester Report evaluated some of the same the [sic] studies that EPA did and found similar results with regard to the increased inflammatory response and increased airway responsiveness of people with asthma when exposed to O_3. The Rochester Report reached the same conclusion that EPA did that this increased responsiveness provides biological plausibility for the respiratory morbidity effects found in epidemiological studies." *Responses* on page 57 includes an extensive quote from the Rochester Report, page 57-58.

I have cited the above material to urge that CARB should engage members of the scientific community in dialogue about health risk assessment *in the same manner as EPA has done,* to find areas of agreement, and to identify areas where further research and better risk assessment methodology are needed. In my judgment (and that of other authors of the Rochester Report), there are still serious problems in how EPA is doing its health risk assessments, and these problems need to be addressed

and remedied. Most importantly, the *Responses* document provides excellent evidence that EPA is not asserting that it can give good estimates of premature deaths avoided by changes in the ozone rule. Rather, EPA is acknowledging the formidable complexity in making such estimates, and EPA makes it clear that its consideration of uncertainties was limited: In the recent proposed Rule, a judgment call was made by EPA's Administrator after extensive consultation with the scientific community, through CASAC and a long process of public meetings and review of technical support documents.

CARB's process of making a central "overall estimate" of premature deaths from $PM_{2.5}$ exposure by taking the median of the median estimates (see the Draft Staff Report, page 24, first paragraph) of the 12 experts in the 2006 EPA Expert Judgment Assessment exercise is really simplistic, and similarly, so are the 5th and 95th percentile estimates. Perhaps such estimates are useful as very crude "ballpark estimates" given alongside a statement that the uncertainty in the central estimate is at least an order of magnitude, as noted in several places in CARB's Draft Staff Report and Presentation. Even better would be an explicit acknowledgement that uncertainty in the mortality impacts becomes greater at lower concentrations. It has not been current CARB practice to make statements about the large uncertainties in its press releases. These uncertainties really need to be explained to decision makers and the public. CARB needs to improve its agency practices in making such disclosures.

The lack of attention to differences between fine particulate matter in California and for the United States as a whole is a serious omission in the CARB Draft Staff Paper and Presentation, and this omission means that the methodology essentially ignores one of the most important sources of uncertainty. This deficiency should be remedied before the Draft Staff Report and the risk methodology are placed into final form.

It would be an excellent idea for CARB to encourage a series of workshops involving leaders in the scientific community (including skeptics and critics, not just those with many publications as principal investigators on studies of air pollution health effects) for dialogue on how risk assessment can be improved. As one of the Panel authoring an now-in-press-for- 2008 National Research Council report, *Public Participation in Environmental Assessment and Decision Making,* as well as a predecessor NRC report (*Understanding Risk: Informing Decisions in a Democratic Society*, 1996), I am part of group of leading scientists calling for more such dialogue in combination with technical analysis of uncertainties and complexities to improve the way that our society manages environmental risks such as the health effects of air pollution.

Doing Expert Elicitation Well:
The Senior Seismic Hazard Analysis Committee Report

I have been asked what good examples there are in the literature for how a segment of the scientific community uses elicitation of probabilities as a representation of expert judgment. Such practice has become widespread among civil engineers responsible for advising on critical structures that are subject to catastrophic failure from

earthquakes (seismic events). Such critical structures include nuclear power plants and a great many bridges and buildings in California. It should be considered remarkable that risk management decisions on retrofitting and other risk management for such structures take place with much less controversy than decisions on regulation of air pollutants. Both areas involve formidable complexity, large uncertainties, high costs, and the potential for extensive injury and death among the public.

The following references may be helpful in providing a perspective on how to deal with uncertainties on which model is correct, and in understanding similarities, differences, and overlap (i.e., degree of independence) in the judgments of a number of experts. The process involved is far more time consuming and costly than the simple exercise carried out by EPA's contractors and selected experts in 2006 on $PM_{2.5}$. It is an indication of what is meant by the term in EPA's *Responses*, "integrated uncertainty analysis." I and others in the professional community can assist CARB (as well as EPA) in how to develop and use such advanced methodology. Of course, the details in assessing human health risk from air pollutants and seismic risk to structures will differ extensively.

References on Seismic Risk Using Expert Judgment

Senior Seismic Hazard Analysis Committee (SSHAC), 1997, R.J. Budnitz (Chair), G. Apostolakis, D.M. Boore, L.S. Cluff, K.J. Coppersmith, C. A. Cornell, and P.A. Morris, "Recommendations for Probabilistic Seismic Hazard Analysis: Guidance on Uncertainties and Use of Experts" Report NUREG/CR-6372, in 2 volumes, Washington D.C., U.S. Nuclear Regulatory Commission. Available at: http://www.osti.gov/bridge/product.biblio.jsp?osti_id=479072

Peer-Reviewed Publication: R.J. Budnitz, G. Apostolakis, D.M. Boore, L.S. Cluff, K.J. Coppersmith, C. A. Cornell, and P.A. Morris, Use of technical expert panels: application to probabilistic seismic hazards, *Risk Analysis* 18:466 (1998).

Peer Review in the form of a 1997 report by the National Research Council: Review of *Recommendations for Probabilistic Seismic Hazard Analysis: Guidance on Uncertainties and Use of Experts*, National Academy Press, http://www.nap.edu/catalog.php?record_id=5487

A Google search will bring up a large number of recent textbooks and professional journal publications commenting on this methodology. It is still evolving, as usually happens in professional practice in both civil engineering and public health.

ARB Should Concern Itself with Forest Fires,
Not Just $PM_{2.5}$ Sources Such as Diesel Engines

In driving from my home in Belmont on the San Francisco Peninsula back and forth to Sacramento for the June 25 workshop, I was very aware of the smoke – another name for fine particulate matter – from the many forest fires in Northern California. As I write these comments nearly two weeks later, the *San Francisco Chronicle* (of July 8, 2008) has a banner headline "The Forecast: Hot and Smoky" at the top of the front

page, and the Op-ed page contains a thoughtful essay from forestry expert Thomas Bonnicksen, "While California burns" http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2008/07/08/EDB911L564.DTL. This essay points out the need to manage the vegetation in California that is subject to wildland fires. ARB should recognize that this source of $PM_{2.5}$ needs much more attention, and it should be working with the California Department of Forestry and Fire Protection to educate the public and state and national leadership on fuel management policies to reduce these fires and the air pollution they cause.

Conclusion

I strongly encourage further discussion and dialogue towards improving the risk assessment process for the health impacts of airborne fine particulate matter. The State of California must make decisions in the face of great uncertainty on the regulation of particulate matter from diesel engines and many other sources. This uncertainty should be fully disclosed – and I applaud the effort to begin doing this in the Draft Staff Report and Presentation of May 22, and I urge that it should be standard practice in ARB press releases and presentations.

I encourage further discussion, publications in the peer-reviewed scientific literature, and reviews by prestigious scientific organizations such as the National Research Council, as has been given to EPA health risk assessment for air pollutants and to the seismic safety expert judgment methodology, in the references above. No such comprehensive review has yet been given to EPA's expert elicitation methodology and its 2006 application to fine PM, although an EPA SAB review is now underway. I was a peer reviewer for EPA's 2006 expert elicitation exercise on fine particulate matter, and my review comments are NOT adequately summarized in the EPA contractor report of 2006 or the CARB Draft Staff Report of May 22, 2008. This discrepancy should be addressed and remedied as the Draft Staff Report is revised. The risk assessment methodology, and particularly the details of expert selection and elicitation of judgment in the form of probability distributions used by EPA for its 2006 exercise, need extensive discussion and further review within the scientific community. In particular, disagreement and dissent should be carefully examined in open workshops. EPA has been much more careful to do this than has CARB, and CARB should improve its practices.

I appreciate this opportunity to participate in the CARB Workshop and to submit these comments.

Engine Manufacturers Association – Joseph L. Suchecki, Chicago IL

July 11, 2008

VIA E-MAIL

Dr. Hein Tran
Research Division
California Air Resources Board
Post Office Box 2815
Sacramento, CA 95812

Re: **EMA Comments on Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California. Draft Staff Report, May 22, 2008**

Dear Dr. Tran:

The Engine Manufacturers Association (EMA) is the international trade association representing the manufacturers of internal combustion engines that power a variety of applications including on-highway trucks and buses, nonroad construction and farm equipment, marine vessels, locomotives, stationary generators, and grounds care and utility equipment. EMA represents our 29 member companies on issues related to emissions, and has worked closely with the California Air Resources Board (ARB) over the years to establish standards and regulations to reduce emissions from internal combustion engines in the state. EMA also has been an active participant on a number of health-related issues including the California ambient air quality standards for PM and ozone as well as diesel PM emission rulemakings.

EMA has reviewed the draft staff report (Draft) dated May 22, 2008, regarding proposed changes to ARB's method to estimate the health effects from PM2.5 and to estimate ambient concentration levels of diesel particulate matter (DPM). EMA provided some preliminary comments and input regarding the Draft at the June 25th workshop and provides here more detailed comments for your consideration and incorporation into the final report. In addition, I am including detailed technical comments on the PM mortality issue prepared by Dr. Suresh Moolgavkar, a consultant to EMA from Exponent, Inc.

The following statements summarize the conclusions of EMA's review:

1. When considering the entire epidemiology literature on the health effects of PM2.5, the proposed concentration response function of 10% increased relative risk per 10 μg increase of PM2.5 is not justified. ARB should reconsider the entire set of epidemiology literature and not rely on one or two studies or the EPA expert elicitation to estimate a relative risk for PM2.5.

2. The proposal to estimate ambient levels of diesel PM from ambient NOx measurements has not been peer reviewed or subjected to the necessary expert

scrutiny. EMA does not believe that there is evidence to support such a simple relationship between ambient NOx concentrations and ambient diesel PM concentrations. Furthermore, even the discussion used to justify the proposal demonstrates the large variability and uncertainty, and the proposed method cannot not be considered valid. No relationship between ambient NOx measurements and ambient diesel PM concentrations should be finalized at this time

3. The draft report is confusing since it mixes discussions regarding health effects attributed to ambient PM2.5 from epidemiology studies with discussions of diesel PM. This leaves the reader and the public with the incorrect and false impression that the epidemiology studies are of diesel PM or that diesel PM is connected to the reported increased mortality reported in the epidemiology studies. The epidemiology studies examine ambient PM from all sources, and there is no scientific evidence to specifically attribute any health effects reported in those studies to diesel PM. The report needs to be revised to correct this issue and make it clear that the two issues being discussed – the relative risk from ambient PM and estimating ambient concentrations of diesel PM – are two separate and distinct issues. EMA recommends that the two topics be separated into different reports.

The rationale for the above conclusions is detailed in EMA's technical comments that follow, as well as the comments of Dr. Moolgavkar. We believe that the draft report needs considerable work and revision before it is finalized or brought back to the Air Resources Board for approval. EMA looks forward to working with you further to resolve these significant issues and to develop a technically sound final report(s).

Sincerely,

Joseph L. Suchecki

Joseph L. Suchecki
Director, Public Affairs

July 11, 2008

State of California
Air Resources Board

Methodology For Estimating	**)**	
Premature Deaths Associated With	**)**	**Draft Staff Report**
Long-term Exposure to Fine	**)**	**May 22, 2008**
Airborne Particulate Matter	**)**	
In California	**)**	

Comments of the
Engine Manufacturers Association

The Engine Manufacturers Association (EMA) submits the following written comments on the draft report entitled "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California" (Draft) dated May22, 2008. EMA is the trade association representing the major manufacturers of internal combustion engines including diesel engines used in mobile source and stationary applications throughout the world. EMA serves as the voice of the industry on engine emissions and regulatory matters with the California Air Resources Board as well as the US EPA. EMA also has actively followed and participated in issues related to the health effects of ambient air pollution and diesel emissions.

The comments that follow address three primary concerns with the draft report and methodology:

1. **The inadequate scientific basis for derivation of an increased relative risk or concentration response function from ambient PM2.5 epidemiology studies,**

2. **The lack of supportive evidence and an adequate peer review for establishing a quantitative relationship between ambient NOx measurements and diesel PM (DPM) levels, and**

3. **The confusion created in the report by attempting to address and commingle discussions of ambient PM health effects with discussions regarding ambient concentrations of DPM.**

Importantly, and in addition to the following comments, EMA is attaching a more lengthy and technical critique of the ambient PM mortality issues prepared by Dr. Suresh Moolgavkar of Exponent as part of our comments. Dr. Moolgavkar's review of the proposed ARB methodology documents a number of significant issues regarding the selective use of the epidemiology literature in deriving the proposed relative risk of mortality associated with ambient PM.

1. The epidemiology literature does not support the relative mortality risk proposed in the Draft, and ARB should revise the report to provide a more balanced and critical review of the literature.

The Draft proposes to revise the methodology used to estimate mortality from long-term exposure to PM 2.5 by raising the relative risk attributable to ambient PM to 10 percent. The rationale for the proposed change is noted in the report as being new and more comprehensive epidemiology studies as well as an expert elicitation conducted by the US EPA. The report further explains that three studies are given significant weight in determining the revised relative risk: the American Cancer Society (ACS) study by Pope et al., the Harvard Six Cities Study by Laden et al., and the enhanced ACS study in California by Jerret et al.

In attempting to derive a revised mortality risk related to ambient PM, ARB does not adequately address the uncertainties and widely-variable results in the PM epidemiology literature but rather relies on the three studies noted above to justify the proposed relationship. Moreover, ARB appears to ignore the uncertainties and technical issues associated with the referenced studies while at the same time ignoring other epidemiology studies that report contrary or lower relative risk estimates. One significant example of this is the dismissal of the epidemiology studies by Enstrom (2005) that reported a much lower risk and even a lack of association between increased mortality and PM2.5 in California. The Enstrom studies are important since they were conducted in California and hence should be particularly relevant to ambient PM levels and composition in the state. Rather than consider the results of those studies, the report dismisses the results.

Additional and further details regarding technical and scientific issues associated with the PM epidemiology studies are included in the accompanying review and comments by Dr. Moolgavkar.

The final report and any estimate of mortality effects associated with exposure to PM2.5 needs to be revised to better reflect the uncertainties and variability in the current literature. In addition, any discussion of morality from ambient PM should be placed in the proper context when reported to the public, including a discussion of the uncertainties and variability in the scientific literature.

2. The proposed method to derive ambient concentrations of DPM from measured NOx levels should not be finalized at this time. Any quantitative relationship between ambient NOx and ambient DPM is highly questionable and not supported in the published literature. The

proposed method must undergone a thorough technical and peer review by appropriate experts on the source apportionment science before being finalized or used.

As part of the re-evaluation of relative risks associated with ambient PM exposure, ARB has proposed a very simple methodology to estimate ambient concentrations of diesel particulate matter (DPM). The proposed method applies a simple constant (specifically, 0.023) to measured ambient levels of NOx to estimate DPM levels. Although simple in concept, there is an inadequate technical and scientific basis for the approach. EMA strongly recommends that the method not be approved or used. Any such relationship needs to first undergo peer review by experts in PM source apportionment and withstand the scrutiny of publication in the scientific literature.

The estimation of DPM in the atmosphere has been an important technical issue for many years since there is no way to directly measure DPM. In addition, there is no specific tracer for DPM, and estimates of its concentration have relied on crude approximations based on elemental carbon measurements or detailed emissions inventory and source apportionment studies. A good review of the issues can be found in the proceeding of a technical meeting on DPM conducted by the Health Effects Institute (HEI 2003)[98]. The conclusion of the three-day workshop was that there is no marker for diesel PM and that the best option may be a combination of markers to derive a diesel signature. That conclusion has not changed.

The ARB proposal to link DPM concentrations to NOx by a simple constant is not valid for the following reasons:

- There is no set or constant relationship between engine-out PM and NOx emissions from diesel engines. The absolute and relative amount of PM emissions and NOx emissions from diesel engines varies greatly depending on the application of the engine, its model and year, and the in-use duty cycle. For example, if one simply looks at emissions standards for diesel engines, there is a great deal of variability in the engine-out or vehicle-out limits for PM and NOx. The emissions limits for NOx are independent of the emissions limits for PM. Table 1 shows the differences in federal emissions standards for various model years and diesel applications. The DPM/NOx emissions ratio varies from 0.007 for 2007 model year trucks to 0.063 for Tier 1 locomotives, and the ratio varies by 9-fold. There cannot be a fixed and constant relationship between NOx and PM in ambient air if the NOx and PM relationship from the sources is neither fixed nor constant.

- Diesel engines are not the only source of NOx in ambient air. There are numerous sources of mobile and stationary NOx emissions in addition to diesel engines, so that any measured NOx concentrations will include NOx from all these other sources. The ambient levels of NOx at the monitoring site therefore

[98] HEI 2003. Improving Estimates of Diesel and Other Emissions for Epidemiologic Studies. Health Effects Institute, Boston, MA. Communication 10. 162pp.

will depend on the number and proximity of other sources of NOx emissions and will vary considerably across geographic areas. Consequently, the different mix of NOx sources will affect the ambient NOx levels both in time and space. Given that there will be a great variability in sources of ambient NOx levels, how can there be a fixed constant ratio between ambient NOx and diesel PM? That ratio must be dependent on the contributions from other NOx local sources. The true or actual DPM/NOx ratio will be larger if there are primarily diesel engine sources in an area and smaller if there are numerous stationary sources in an area. Unless there is a constant and uniform mix of sources throughout CA and across time, the DPM/NOx ratio cannot be constant. This fact is totally contradictory to the proposed ARB method.

Table 1. Representative NOx and PM emissions standards for Diesel Engines

Application	Model Year	NOx Standard	PM Standard	PM/NOx Ratio
On-Highway	2004	2.0	0.10	0.050
On-Highway	2007	1.4	0.01	0.007
Nonroad	Tier 2	6.6	0.2	0.030
Nonroad	Tier 3	4.0	0.20	0.050
Locomotive	Tier 0	9.5	0.60	0.063
Locomotive	Tier 2	5.5	0.20	0.036
Marine	Tier 2, Cat 1	7.2	0.20	0.028
Marine	Tier 2, Cat 2	7.2	0.40	0.051

- The assumptions used by CARB to derive the proposed ratio are not valid. In the discussion of the derivation of the proposed constant in Appendix 3, CARB makes two assumptions regarding the proposed constant. First, based on the tracer species method, CARB assumes that NOx is a tracer for DPM that can be used alone with a scaling factor that is independent of location. Both assumptions needed to validate the tracer method are not true. NOx is not a unique tracer for DPM since there are many other sources of NOx emissions in addition to atmospheric processes that affect its ambient levels. Second, as noted above, the scaling factor is not independent of location. The scaling factor will depend on the local and regional sources of ambient NOx and DPM.

  Second, in discussing recent analyses by Lawrence Livermore Laboratory and ARB's Monitoring and Laboratory Division, ARB makes an assumption that all fossil elemental carbon is from diesel emissions. This is certainly not the case. As noted in the HEI report (HEI 2003) and in numerous other studies, elemental carbon emissions are not unique to diesel and are not considered a marker for diesel emissions. Consequently, the analysis relating to this point is incorrect.

- Additional information and data on the relationship between NOx emissions and PM emissions from diesel vehicles can be found in the recent Gasoline-Diesel PM Split study. This study provides measurements of NOx and PM emissions from in-use

diesel engines (study results available on the CRC website, Projects E-55/59, E-75)[99]. The results of those studies again demonstrate that there is no constant relationship between real-world NOx and PM emissions from diesel engines. For example, for post-1993 heavy-duty vehicles tested the PM/NOx ratio varies over 13 observations from 0.0002 to 0.06 (Report No 07.10.00/9452.000, Figure B-47). Although those study results represent real world, in-use emissions, they still do not reflect the variability in NOx and PM emissions from diesel engines since the actual emissions depend heavily on duty cycle and specific application. Again, this clearly demonstrates that actual diesel emissions are not uniform or constant. These data strongly argue against the possibility that a single scaling factor can be used for all diesel emissions.

- The scaling factor chosen by ARB is arbitrary with no scientific rationale for its selection. The scaling factor was determined by looking at DPM/NOx ratios from two long-term source apportionment studies and appears to rely heavily on the data obtained from the Children's Health Study (1995). Figure 2, Appendix 1 in the Draft is used to develop the scaling factor of 0.023 from a regression analysis of those data as well as information from emissions inventory data. However, ARB also discusses a number of studies such as the DRI San Joaquin Valley Study, the gasoline-diesel split studies by Shauer and Fujita, and the Livermore studies that show a lower scaling factor on the order of 0.016. In fact, Figure 4 of the Appendix shows that very different results regarding DPM levels were obtained from the gasoline-diesel split study by Fujita and Schauer using the same data.

  In the discussion of the Schauer-Fujita work, ARB admits that there is no *a priori* information about which method is "correct" or valid. If there is no information about which result is correct or valid, and ARB has several studies showing different results – i.e., perhaps the scaling factor is 0.023 or 0.015 - there is no rational way to select a DPM/NOx scaling factor at all. Why did the authors choose 0.023 when other studies reviewed reported a value of 0.015? The scaling factor selected appears to be totally arbitrary and cannot be justified by the scientific data reviewed.

- Perhaps most importantly, the data and studies used to develop the scaling factor are outdated, do not represent the current mix of diesel engine sources in-use today, and are no longer valid for deriving the scaling factor. Even if the methodology used by ARB to develop the scaling factor was valid, which it is not, the data on diesel emissions used are no longer valid for estimating DPM today or in the future. The primary database used to derive the scaling factor and DPM/NOx ratio is from the 1995 Children's Health Study. There have been many significant changes in emission regulations, diesel fuels, and diesel engine technology since 1995, and those emissions characteristics do not represent current or future PM or NOx emissions from diesel engines.

  For example, the in-use diesel fleet in 1995 had significantly different emissions characteristics compared to today since it predates major emissions reductions for heavy-duty on-highway engines that became effective in 1998, 2004 and 2007. The

[99] http://www.crcao.com/publications/emissions/index.html

1995 fleet data also reflect emissions from a non-regulated nonroad engine fleet. The first nonroad, Tier 1 emissions standards began implementation in 2000. Since that time, emissions from diesel vehicles and equipment have declined by over 90%, and in the case of on-highway PM emissions, by over 99%. In addition, ARB has started to implement retrofit requirements to reduce diesel PM from existing stationary, on-highway, and nonroad vehicles and equipment.

With the significant effort to reduce emissions since 1995, and given that there has been considerable fleet-turnover and retrofit in the last 13 years in CA, today's NOx and PM emissions characteristic are very much different than those that were present in 1995. Consequently, any scaling factor or relationship between NOx and DPM based on 1995 data is not valid today and certainly cannot reflect ambient air quality relationships present today or in the future in CA. The proposed scaling factor based on these data cannot be valid to estimate current DPM levels.

- It is not clear what data where used to derive the scaling factor. In looking at the Children's Health Report from 1995, it is not clear what data were used to develop Figure 1 in Appendix 3. The CHS report provided average NOx data over several years, and Schauer estimated diesel PM contributions for 1995. The derivation of Figure 1 needs to be better explained as to what data from the CHS report were used.

- DPM levels estimated through use of the proposed scaling factor in the draft report do not appear to agree with other source apportionment methods used to estimate DPM. ARB claims that the results of using the scaling factor agree well with other studies. We disagree. Although perhaps providing a ballpark estimate within the range of other studies, the use of the scaling factor does not provide an accurate estimate of DPM. For example, Table 1 of Appendix 3 indicates that the estimate for the South

Coast Air basin is 2.90 $\mu g/m^3$. However, the 2005 inventory estimate used by the AQMD in MATES III is 3.25, and the CMB estimate is 3.52-3.84. Similarly, EMA estimated DPM concentrations using the proposed method and annual average NOx levels reported in the CHS report and compared them to the source apportionment results reported by Schauer (2003)[100]. As shown in Table 2 below, there was not good agreement with the results between the two methods.

[100] Manchester, JB, JJ Schauer, and GR Cass. 2003. The Distribution of Particle-Phase Organic Compounds in the Atmosphere and Their Use for Source Apportionment during the Southern California Children's Health Study. J Air Waste Manag Assoc, 53: 1065-1079.

Table 2. DPM Estimates using the proposed ARB method and Shauer Source Apportionment Approach

Location	ARB Scaling Method DPM	Schauer Apportionment DPM
Atascadero	0.80	1.02
Lompac	0.22	0.36
San Dimas	2.8	3.92
Riverside	1.77	2.41
Long Beach	2.76	3.59

From the above brief review of the data, it does not appear that the scaling factor provides results similar to more scientifically acceptable methods.

Considering the above issues surrounding the development and use of a scaling factor relating DPM to NOx, EMA strongly believes that the proposed method is not valid and should not be finalized or used at this time. There is simply insufficient and contrary evidence to validate the proposed model and scaling factor. Even if such a relationship were possible, the current methods and approach have not been validated or peer-reviewed by the scientific community nor has it been peer-reviewed in the published literature. The significant departure from the currently accepted methods of estimating DPM through source apportionment methods cannot be approved without a thorough and complete review. Those reviews need to take place before the method is finalized or put into practice.

EMA believes that if ARB is interested in pursuing this method further, an acceptable approach would be to have a technical workshop on the method with participation by the recognized experts in the source apportionment field. EMA would be happy to work together with ARB on such a workshop to discuss the issues surrounding the proposal and the general topic of diesel PM source apportionment.

3. The discussion of the relative risk from ambient PM should be separated from the topic of estimating DPM concentrations to avoid the implication that diesel PM is uniquely associated with any ambient PM health effects.

The draft report is entitled "Methodology for Estimating Premature Deaths Associated with Long-term Exposure to Fine Airborne Particulate Matter in California**",** yet it really deals with two separate and distinct topics: First, as the title implies, revising the proposed relative risk of mortality from ambient PM; and second, estimating the ambient concentration of DPM. The two are not related and should be discussed in separate reports.

The problem with the current document is that it mixes discussions about the health effects and reported mortality estimates of ambient PM with a discussion of diesel PM. Because of the way the two topics are presented, the reader can be mislead into thinking that the mortality issues from PM are somehow linked to, or primarily caused

by, diesel PM. This is clearly not the case. First, the epidemiology studies discussed and referenced are not studies related to DPM, but ambient PM from all sources. Secondly, as noted in other regulatory documents by both the US EPA and CARB, there is no indication in the literature as to which components or sources of PM may be linked to any health effects. That is, there is no evidence to suggest that PM from diesel sources is either more or less toxic that PM from other sources. Further, if the report is supposed to be addressing a methodology to estimate premature deaths from ambient PM, there is no reason to include a separate discussion of ambient DPM. ARB does not need to estimate ambient DPM since ambient PM levels can be measured directly.

EMA recommends that the two issues be separated and addressed in different reports, one dealing with mortality estimates from ambient PM, and a second dealing with issues related to estimating ambient levels of DPM. There simply is no need to have both topics covered in the same report. In addition, as noted above, EMA does not believe that the DPM estimation methodology is valid nor is it ready to be finalized. Separating the two topics would allow ARB to proceed with the ambient PM mortality report and methodology as scheduled while allowing additional time for a necessary peer review of the DPM estimation method.

Exponent, Inc. and consultant to EMA, Suresh H. Moolgavkar

Draft Staff Report, May 22, 2008

Review of 'Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California'

California Environmental Protection Agency, Air Resources Board

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EXECUTIVE SUMMARY

This document is a critique of the California Air Resources Board (CARB) report 'Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California'. That report describes a proposed approach to estimating the number of deaths associated with fine particulate matter (PM) pollution in California with particular emphasis on emissions from diesel engines. The report begins with a brief review of the literature to derive a concentration-response (CR) function for fine PM associated mortality. The chosen CR function is based on an expert elicitation report commissioned by the USEPA in 2006. The methodology proposed by the California Air Resources Board (CARB) is seriously flawed and cannot be used as a basis for estimating the number of deaths attributable to fine PM pollution in California.

1 The literature review is seriously biased. The CARB fails to note the limitations of the studies it relies on while giving short shrift to studies that report findings contrary to the opinions expressed in this document. It omits discussion of an important recent study suggesting that the reported associations between fine PM and mortality could be due to confounding.
2 In evaluating the studies considered, the CARB does not apply its own stated criteria to studies that support its position.
3 The CARB fails to note the serious methodological limitations in the long-term studies of the association of fine PM with mortality. In particular, these studies associate mortality with contemporaneous levels of air pollution. If indeed air pollution is associated with mortality, then long-term exposure, including exposure in the past when concentrations were much higher, is surely important. The consequence of considering only contemporaneous exposure is to inflate the estimate of risk associated with a unit concentration of exposure.
4 The choice of a CR function based on an expert elicitation is totally inappropriate. There are formal methods of meta-analyses that can be used to combine the results of multiple epidemiological studies to arrive at a single estimate of risk.

The individual members of the expert elicitation panel employed their own judgment to perform a subjective 'meta-analysis'. To then combine these subjective 'meta-analyses' in another subjective 'meta-analysis' to derive a single CR function has no basis in science.

5 The CARB appears not to have considered the multiple sources of uncertainty involved in its risk assessments for diesel particulates.

In its revision, the CARB should address these concerns. In particular, all relevant epidemiologic studies should be considered and their strengths and weaknesses discussed. Alternative interpretation of the reported findings of these studies should also be considered. Many publications discussing the primary epidemiologic studies have appeared in the peer-reviewed literature but have been ignored by the CARB. Finally, any risk assessment should be based on a proper consideration of the primary epidemiologic studies and not on the range of estimates in an expert elicitation report. The myriad sources of uncertainty, including those involved in estimating the concentration of diesel particulates, should be acknowledged and considered in the risk assessment.

Introduction

This California Air Resources Board (CARB) report presents methodology for estimating the number of premature deaths associated with long-term exposure to fine particulate matter (PM) in California. Much of the report consists of a review of the literature to derive a concentration-response (CR) function for risk assessment. Ultimately, the CR function is based on an expert elicitation commissioned by the US EPA. In the second part of the report, this CR function is applied to estimate the benefits that would accrue under various roll-back scenarios. The report also presents estimates of the number of premature deaths attributable to exposure to diesel exhaust. There are a number of problems with this report, which are summarized here and discussed in detail below.

1. The report does not present a fair and balanced review of the literature. Papers supporting the agency position are given prominent play with little discussion of their limitations and deficiencies. Papers that report findings contrary to the agency position are given short shrift. The most egregious example of this unbalanced treatment is the discussion of the mortality study in California conducted by Enstrom. This study is dismissed for, among other things, not considering environmental tobacco smoke in the analyses, while the agency completely ignores the fact that neither the six cities studies nor the studies based on the American Cancer Society (ACS) cohort, which the agency relies heavily on, had information on environmental tobacco smoke. In fact, smoking, a potentially strong confounder in long-term studies of air pollution, is addressed in only the most rudimentary fashion in all studies that the CARB relies on. This issue is discussed in detail below along with other examples of unbalanced treatment of the published literature.

2. The agency does not use its own criteria for evaluation of the studies it considers. For example, the report says (page 22) that studies "...should ideally have controlled for co-pollutants..." but ignores the fact that the six cities studies (Dockery et al., 1993; Laden et al., 2006) could not control for co-pollutants and that neither the original ACS study (Pope et al., 1995) nor extensions of it (Pope et al., 2002, 2004) controlled for co-pollutants even though such control was possible. Finally, the CARB

ignores the results when including co-pollutants yields results at odds with its position. For example, the CARB ignores the results of the Krewski re-analysis of the original ACS study, which shows quite clearly that it is SO_2 and not fine PM that is associated with mortality in joint pollutant analyses. These studies are central to the risk assessments presented in the CARB report. More details are provided below.

3. The CARB fails to cite important recent studies that arrive at conclusions not consonant with its position. For example, the study by Janes et al. (2007) suggesting that the reported associations between fine PM and mortality could be due to uncontrolled confounding is not discussed. Other examples of studies that have evaluated the epidemiologic data and have come to conclusions contrary to those held by the CARB are cited throughout this review. These studies have not been considered by the CARB.

4. The CARB's discussion of uncertainty is incomplete and does not address some important sources of uncertainty.

5. The agency bases its risk assessments on the opinions expressed by members of an expert elicitation panel assembled by the US EPA. When the actual epidemiology studies are available for review there seems little scientific justification to rely on an expert panel, members of which bring their own particular biases to the table. This issue is discussed in more detail below.

The CARB report does not present a fair and balanced review of the literature.
The CARB report does not acknowledge that while a number of short-term and long-term studies of air pollution report associations between current ambient levels of air pollution and adverse impacts on human health, including mortality, many other studies do not report such associations. The report should also acknowledge that model choice, including the choice of confounders included in analyses, can profoundly influence the results. Since the report relies largely on long term studies of the association between fine PM and mortality, these studies are discussed here. Among these studies, the agency relies most heavily on studies based on the six cities cohort and studies based on the ACS cohort. These studies are discussed in this review to highlight some of their limitations not acknowledged by the agency. Some studies given short shrift by the agency because of supposed serious limitations are also discussed here to highlight the fact that they have considerable strengths and deserve more serious consideration. In particular, the Enstrom study, conducted in California, is clearly highly relevant. Before discussing the individual studies, the major limitations of the principal statistical tool used for the analyses of all long-term studies of air pollution and mortality, the Cox proportional hazards model, are discussed.

<u>Fundamental limitations of the proportional hazards model</u>
The long-term studies used Cox proportional hazards regression models for data analyses. As has been pointed out in Moolgavkar (2006, 2007), the Cox proportional hazards model has a number of limitations when it is used for the detection of small risks in epidemiologic data, particularly in the presence of potentially strong confounders. Among others, there are two fundamental assumptions that have been made in the application of the Cox model to the analyses of long-term air pollution studies. The first assumption is that the relative risks for both the effects of air pollution, *e.g.*, fine PM, and the effects of potential confounders, such as cigarette smoking remain constant with time. The second assumption is that the relative risks remain

constant with age. This assumption requires that the relative risk of death due to air pollution is the same at all ages. It also requires that the relative risk for confounders remains constant with age. For example, the relative risk of death for smokers who smoke 40 cigarettes per day is assumed to be the same at all ages. Both these assumptions are false (Moolgavkar, 2006, 2007), both for the effects of fine PM and of cigarette smoke on mortality.

With respect to the first assumption regarding fine PM, both the Laden *et al*. (2006) and the Enstrom (2005) studies show that the relative risks decrease with time, *i.e*., the RRs are smaller in the later time periods. With respect to the second assumption regarding fine PM, it is clear from the Villeneuve *et al.* (2002) study that the relative risks associated with fine PM are not the same at all ages. In contrast, the Cox model as used for the analyses of these studies assumes that the RR remains constant over time and with age. However, even if both assumptions were to hold for exposure to fine PM, serious bias could result if they did not hold for a potentially strong confounder of the fine PM-mortality association, such as cigarette smoking. The first assumption most definitely does not hold for cigarette smoking: we know that, for a given daily level of smoking, the relative risk of lung cancer does not remain constant with time, but is strongly dependent on duration of smoking (Rachet *et al*., 2004). The second assumption, constancy of relative risk with age, does not hold for cigarette smoking either. In fact, it is clear from analyses of the ACS I study that proportionality of hazards for cigarette smoking does not hold for lung cancer, cardiovascular or total mortality (Burns *et al*., Table 11, 1996). Figure 1 below shows the relative risks for total mortality among smokers smoking 40 or more cigarettes per day as a function of age. It is clear that the relative risk does not remain constant with age. In fact, it is clear from the epidemiologic data that the risk associated with smoking depends in a complicated way on the intensity of smoking, the duration of smoking, and, among ex-smokers, the time since cessation of smoking. None of the long-term studies, including the six cities and ACS studies relied on by the CARB, had information on all these factors. These studies had information on smoking histories only at the beginning of the period of study and made no attempt to model the evolution of smoking-associated risk with time on study. Thus, these studies adjusted smoking only very crudely.

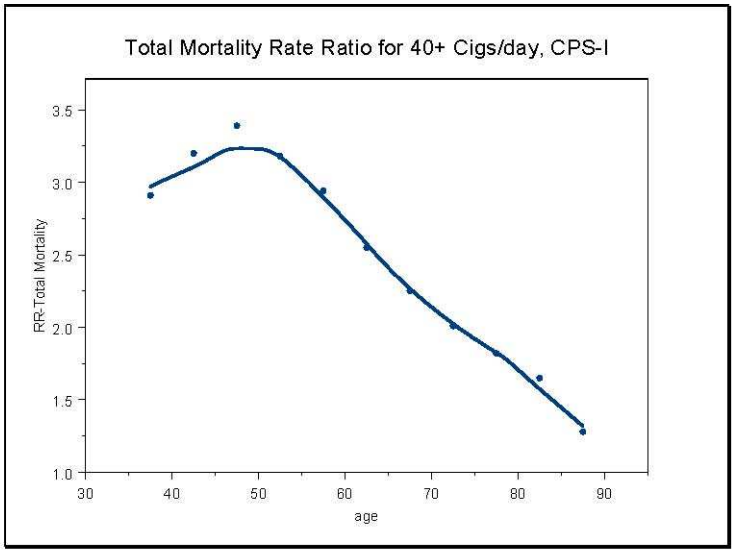

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Figure 1: Rate ratios (relative risks) for total mortality among smokers w e smoke 40 or more cigarettes per day in the first American Cancer Society

estimates of fine PM effects found in long-term studies. This concern applies equally to studies that report associations between fine PM and mortality (*e.g.*, the Six Cities and ACS II studies and extensions) and studies that do not report such associations (*e.g.,* Lipfert *et al.*, 2000, 2006a,b; Enstrom, 2005).

Study (CPS I). Note that the proportional hazards model, which was the main tool for analyses of the long-term studies of air pollution, makes the assumption that the relative risk is constant with age, an assumption that is clearly false. Figure reconstructed from Table 11 in Burns *et al*. (1996).

Use of the Cox proportional hazards model when the basic assumptions of the model are violated can have serious consequences for the inferences drawn from the data. For example, Prentice *et al.* (2005a, 2005b) have suggested that departures from the basic assumptions of the proportional hazards model may partly explain the discrepant findings between observational epidemiological studies of postmenopausal hormone therapy and the recently concluded randomized trial of estrogen plus progestin in the Women's Health Initiative.

Finally, the Cox model as used in these analyses regresses mortality against contemporary levels of air pollution in cities. If indeed air pollution is associated with mortality, then long-term exposure, including exposure in the past when concentrations were much higher, is surely important. The consequence of considering only contemporaneous exposure is to inflate the estimate of risk associated with a unit concentration of exposure.
All the long-term studies of fine PM use the Cox proportional hazards model for their analyses and therefore suffer from the same flawed assumptions. The CARB experts seem unaware of this fundamental problem. But, even if this problem is ignored, it is clear that the various long-term studies of air pollution and mortality report highly inconsistent results as I discuss below.

A. Studies based on the six cities cohort

The CARB relies heavily on the original six cities study (Dockery et al., 1993) and a recent update (Laden et al., 2006). In fact, for the original six cities study, the CARB claims that it, along with the first study based on the ACS cohort, "... provided compelling evidence of mortality effects from long-term fine particulate air pollution." The CARB makes this sweeping statement even though the six cities study could not, because of the small number of cities involved, consider confounding by co-pollutants, which, by its own reckoning is important in assessing any air pollution study (page 22). The CARB lavishes praise on this study saying, "[t]he strengths of the Harvard Six Cities Study were its elegant and relatively balanced study design, ...,and the ability to present core results in a straightforward graphical format." I am not sure that elegance and relative balance in study design (whatever that means) are objective criteria that can be used to assess the strength of a study. I do not view the ability to present results in graphical format a strength either. However, the inability to consider confounding by co-pollutants is very definitely a major limitation not recognized by the CARB.

In the Harvard Six Cities Study, a random sample of over 8,000 adults was selected from six cities in Northeastern and Midwestern United States. Proportional hazards regression modeling, a commonly used statistical method as noted above, was used for analyses. Relative risks for mortality for residence in a particular city were estimated after adjustment for cigarette smoking, education and body mass index. Although much is made of the control of smoking on an individual level as a strength of this study, this control is crude as I have discussed above. In the city with the highest level of pollution as measured by levels of fine PM, the adjusted death rate was 26% higher than in the city with the lowest pollution. If the six cities are ranked in order of adjusted death rates from lowest to highest, and if this ordering is compared with the ordering imposed by various indices of air pollution, the agreement seems good, particularly if fine PM is used as an index of air pollution. Thus, in this study, there appears to be good correlation between levels of fine PM pollution and death rates, after adjustment, albeit crude, for some important potential confounders measured on the individual level.

However, as Krewski *et al.* (2000, page 223) note in their re-analyses:
"The Six Cities Study, with its small number of cities and high degree of correlation among the air pollutants monitored, did not permit a clear distinction among the effects of gaseous and fine particle pollutants. Indeed, estimates of the relative risk of mortality from all causes were similar for exposure to fine particles, sulfate, sulfur dioxide, and nitrogen dioxide. Of the gaseous copollutants in the Six Cities Study, *only ozone did not display an association with mortality."* (emphasis added).

In other words, sulfur dioxide (SO_2) and nitrogen dioxide (NO_2) are also correlated with mortality, but ozone is not. Moreover, the correlation may not reflect a causal association between air pollution and mortality at all. Rather, it may reflect uncontrolled confounding by ecologic covariates, such as socio-economic status. Thus, the correlation
observed in the six cities study does not even provide support for a causal association between exposure to air pollution generally and mortality, much less a causal association between fine PM and mortality.

<u>Update of Six Cities Study (Laden *et al.*, 2006)</u>. In this recent paper, relied upon by the CARB, the authors extended follow-up of the six cities cohort by eight years to 1998. They also used proportional hazards modeling to analyze the extended follow-up data and concluded that "[i]mproved overall mortality was associated with decreased mean $PM_{2.5}$…" CARB cites this paper in support of the contention that cleaner air leads to health benefits. However, Table 2 in the Laden paper shows clearly that, in the period 1990-1998, mortality rates are not higher in cities with high concentrations of fine PM. The following table is constructed from the results shown in Tables 1 and 2 in Laden *et al*.

Table 1. Results compiled from tables 1 and 2 of Laden *et al*. 2006. The six cities in the study are arranged in order of increasing average concentrations of fine PM over the period 1990-1998. The relative risks are reported in the last column. There is no indication of a systematic increase in risk with increasing fine PM concentration.

If fine PM were associated with mortality at any concentration, one would expect to see higher death rates in the cities with higher concentrations of fine PM even in the follow-up period. But this result was not observed, which suggests strongly that, either the result reported in the original six cities study was simply a statistical artifact or that there is a concentration below which no fine PM association with mortality is discernible in this study. Furthermore, in another example of unbalanced treatment of the literature, the CARB faults Enstrom's study in California for having sparse exposure measurements but fails to note that Laden et al. had exposure measurements only over a limited period of time. For the rest of the period covered by their study they used regression equations to estimate fine PM concentrations. This procedure introduces a great deal of uncertainty in their analyses and is a major limitation of the study not recognized by the CARB.

B. Studies based on ACS II

The ACS II study (Pope *et al.*, 1995) was a much larger study than the six cities study, involving 151 cities and more than 500,000 individuals. The design of the ACS II Study was similar to the design of the six cities study. The study was undertaken specifically to test the major hypothesis raised by the six cities study – that fine PM was associated with mortality. With 151 cities in the data base, there was a real opportunity to adjust ecologic confounders, particularly co-pollutants. The investigators did not do so, however, and did not explain why they failed to do so. Given the opportunity to address the obvious deficiency of the six cities study, this omission is particularly troublesome. The failure to consider confounding by co-pollutants is a major deficiency of this study and casts doubt on the reported association between fine PM and mortality.

CITY	**Average fine PM concentration in micrograms per cubic meter.**	**Relative Risk**
PORTAGE	10.2	1.00
WATERTOWN	12.1	0.82
TOPEKA	13.1	1.01
ST. LOUIS	13.4	0.96
HARRIMAN	18.1	1.10
STEUBENVILLE	22.0	1.06

One of the criticisms of the original analyses of the ACS II data by Pope *et al.* 1995 was that ecologic confounders were not considered. Therefore, the second phase of the HEI re-analyses (Krewski *et al*., 2000) explicitly considered a number of ecologic confounders, including co-pollutants. The main findings of these analyses were (1) substantial attenuation of the fine PM associations when SO_2 was considered simultaneously in two-pollutant analyses (*i.e.*, fine PM associations got weaker when SO_2 was taken into account), which indicates that it is SO_2 and not fine PM that is associated with mortality in this data set; (2) attenuation of the PM effect when spatial correlation[1] was considered; and (3) modification of the PM association by level of education so that the association was observed only in the sub-population with a high school education or less. It is puzzling that fine PM pollution would increase mortality risk only among those individuals with less than a high school education and suggests that the fine PM mortality association found in this study is spurious. I consider these findings in more detail below.

[1] Spatial correlation occurs because cities in close proximity to one another share similar features. For example, death rates in the twin cities of Minneapolis and St. Paul are correlated. This could be because they have similar pollution profiles, but could also be due to other shared characteristics, such as life-style and socioeconomic factors.

The CARB fails to note the fact that, in these re-analyses, fine PM is ***not*** the pollutant most strongly associated with mortality. When SO_2 was considered along with PM in the model for all-cause mortality, the coefficient for sulfates was reduced to less than one third of its original value, the coefficient for fine PM was reduced to one sixth of its original value, and both became statistically insignificant. In contrast, the coefficient for SO_2 remained statistically significant and was not much attenuated by the inclusion of either fine PM or sulfates in two-pollutant models. The general scientific consensus is that there is no plausible biological mechanism by which exposure to SO_2 could lead to increased mortality.
Therefore, the association of SO_2 with mortality in these re-analyses remains unexplained.

Regarding the second finding of the Krewski re-analyses, the CARB fails to note that the adjustment of spatial correlations (see footnote 1) in the data leads to a weakening or reduction of fine PM coefficients, rendering many of them insignificant. Moreover, the SO_2 coefficients are much less attenuated by the spatial analyses. As Smith *et al.* (2001) point out, consideration of spatial correlations weakened the fine PM coefficients to a much greater extent than the coefficients for SO_2, "[f]or example, in an analysis including both sulfate particles and SO_2 (Krewski *et al.* (2000), pp. 210-211), the RR for sulfate dropped from 1.20 to 1.08 (95% CI: 0.91 to 1.28) although that for SO_2 was less affected (RR from 1.35 to 1.31; CI 1.12 to 1.50)." In fact, Krewski *et al*., referring to the attenuation of estimated coefficients after spatial adjustment, say (page 211), "[j]oint modeling produced a larger reduction in the sulfate-associated relative risk of mortality (1.20 to 1.08) than in the sulfur dioxide relative risk (1.35 to 1.31)." Thus, the spatial analyses confirm that the association of fine PM with mortality is much less robust than is the association of SO_2 with mortality. Remarking on the spatial models used in the re-analyses, Smith *et al.* say, "[i]n spite of the incomplete nature of the spatial analysis, it did have a significant impact on the results. If such a substantial change is possible

through only a one-parameter addition to the model, it can only be speculated what would happen with more realistic spatial models."

Third, Krewski *et al.* found that the fine PM association with mortality was restricted to the sub-population with a high school education or less. This finding was confirmed by Pope *et al.* (2002) in the extended follow-up of the ACS II study. The authors of Pope *et al.* (2002) speculated that those with low socioeconomic status are particularly susceptible to fine PM pollution. However, other interpretations are more plausible. For example, socio-economic factors, which are known to influence mortality strongly, may not have been adequately controlled as possible confounders. Other explanations for this finding have been provided by Grahame & Schlesinger (2005).

The CARB asserts, "The reanalysis demonstrated the robustness of the PM-mortality risk estimates to many alternative model formulations." (page 5). To the contrary, the brief discussion above demonstrates convincingly that the estimate of the mortality impact of fine PM in the Krewski reanalyses clearly depends on the statistical model used, including which copollutant is considered. Of the many estimates reported, there is really no scientific justification for choosing the one that Pope & Dockery chose to present in their table reproduced in the CARB report. The internal consistency of a study is also important in deciding whether or not specific estimates from that study can be used to measure reliably the impact of air pollution on human health. For example, the Krewski reanalysis reports statistically significant protective effects of ozone and NO_2 on mortality (Krewski et al., 2000, tables 34, 37). Clearly these findings are not credible as they fly in the face of biology. These findings cast doubt on the conclusion that a particular fine PM coefficient from that study would yield reliable estimates of mortality.

In a study of the ACS II cohort with extended follow-up data that followed the Krewski re-analyses, Pope *et al*. (2002) reported significant associations between fine PM and oxides of sulfur with all-cause, cardiovascular, and lung cancer mortality. The risks for all-cause and cardiovascular mortality are lower than those reported in the original 1995 analysis; whereas the risk for lung cancer mortality is considerably higher. Surprisingly, despite the findings by Krewski *et al.*, no joint pollutant analyses of PM and SO_2 were carried out. Thus, Pope *et al.* (2002) simply leaves unaddressed the question of which of these two pollutant classes is more strongly associated with mortality. Yet, the need to evaluate the two pollutants is probably the single most important finding in the Krewski ACS II re-analyses. The Pope *et al.* (2002) paper also reported a ***statistically significant negative*** association between CO and total, cardiopulmonary, and lung cancer mortality.

This is a surprising result in view of the biological plausibility of an association between CO and cardiopulmonary mortality, and also time-series studies that have reported ***positive*** associations between CO and both total and cardiopulmonary mortality (e.g., Moolgavkar, 2003b). This finding clearly casts doubt on the reliability of the other results in the Pope *et al*. (2002) paper, including the reported fine PM association with mortality.

In a second update of the ACS II study, Pope et al. (2004) examined the association

between fine PM and cardiovascular mortality. They concluded that "[a]lthough smoking is a much larger risk factor for cardiovascular disease mortality, exposure to fine PM imposes additional effects that seem to be at least additive if not synergistic with smoking." They concluded also that the association of fine PM with respiratory mortality is weak. In fact, however, these authors found a statistically significant protective association between exposure to fine PM and respiratory mortality, a finding that makes little biological sense and casts doubt on their other reported findings. Moreover, their reported finding of a possible synergistic action of fine PM and smoking in their association with mortality is at odds with the reported results of their earlier paper (Pope et al., 2002), which I have briefly discussed above. In that publication, the authors reported that fine PM associated mortality risks were ***lower*** among smokers than among non-smokers. Finally, the authors did not consider any pollutant other than fine PM in these analyses.

In view of the inconsistencies reported in the studies based on the ACS cohort, how can any of the coefficients be used to derive reliable quantitative estimates of the impact of fine PM on mortality?

The discussion above suggests strongly that, even if the association between ambient fine PM and mortality is real in these long-term studies, the magnitude of the association has been greatly exaggerated, as a result of either inadequate control of confounding, use of inappropriate statistical models, and consideration of only contemporaneous levels of air pollution, as I have discussed above. If the reported positive associations between fine PM and mortality in these re-analyses are due to uncontrolled confounding, what are the possible confounders? Two strong candidates are changing smoking habits and changing life-style factors. We know that there have been profound changes in life-style and smoking habits over the period of this study. Healthier life-styles – eating better, exercising more, smoking less – are more likely to have been adopted in the more affluent, better-educated communities, which are also exposed to lower pollution concentrations. Thus, the reported association between either fine PM or SO_2 and mortality may simply reflect the impact of changing life-style factors, including changes in smoking habits, on mortality. In particular, smoking is such a strong risk factor for mortality that controlling changing habits well enough to assure absence of residual confounding is extremely difficult. The strong effect modification by level of education in the Krewski re-analyses suggests that socioeconomic and related factors, such as changes in smoking habits and life-style, need very careful control in these studies.

<u>Extended ACS II Study in Los Angeles (Jerrett *et al.*, 2005)</u>. Jerrett *et al.* extracted data on almost 23,000 subjects in the Los Angeles area from the ACS cohort for the period 1982–2000, with more than 5,000 deaths. Pollution exposures were interpolated from 23 fine PM and 42 ozone fixed-site monitors. After controlling for 44 individual risk factors
for mortality (*e.g.*, smoking), they reported a significantly increased risk of mortality associated with fine PM for all-cause, ischemic heart disease, and lung cancer mortality.

The only joint pollutant analyses conducted were with ozone, and the authors conclude that the PM results were robust to adjustments for ozone and expressway exposure.

The authors also state that the magnitude of fine PM effects are about three times as large as those found in earlier studies, the clear implication being that the better exposure estimates obtained by interpolation of the pollution data "suggest the chronic health effects associated with within-city gradients in exposure to $PM_{2.5}$ may be even larger than previously reported across metropolitan areas." However, when contextual covariates related to socioeconomic status were included in the analyses, the associations of fine PM with total, ischemic heart disease, and lung cancer mortality were substantially attenuated and became either insignificant or only borderline significant. Moreover, although SO_2 was strongly associated with mortality in the Krewski re-analyses, surprisingly Jerrett *et al.* considered no co-pollutants other than ozone. This omission is significant because in time-series analyses in Los Angeles, both CO and SO_2 have been found to be associated with mortality even though concentrations of SO_2 are low (Moolgavkar, 2000, 2003a, b). Particularly in view of the strong association reported for ischemic heart disease in this study, CO, which is known to be a cardiac toxin, should have been considered as a potential confounder. Finally, the RR for lung cancer in this study (1.44 without the contextual covariates) is much higher than that reported in any of the previous analyses of the ACS II cohort and appears to be much too high to be biologically plausible. Unfortunately, the paper does not present the relative risks associated with strong risk factors, such as cigarette smoking, estimated in this study.

In epidemiological studies, the estimated risks from such factors are often used as a 'reality check' of whether the analyses yield reasonable estimates of well-studied risk factors.
Unexpectedly, Jerrett et al. report extraordinarily high fine PM associated risks (RR of around 2.5) for death from endocrine disorders including diabetes. It is not clear how fine PM pollution could impose such high risks of death from these causes. A plausible explanation is that fine PM concentrations at the zip code level are highly correlated with socio-economic status and the high death rates in areas of high pollution, which are probably zip codes with low SES, reflect quality of care issues. Thus, by considering pollution concentrations at the zip code level, the Jerrett et al. study may actually be picking up the effect of SES, which is potentially a strong confounder of air pollution in mortality studies.

C. The Washington University-EPRI Veterans Study (Lipfert *et al.*, 2000)

The Veterans Study is another large long-term study of air pollution and all-cause mortality. The cohort consists of approximately 50,000 U.S. veterans who were diagnosed with hypertension in the mid 1970s. The cohort had an average age of about 51 at recruitment, is all male, and is about 65% white and 35% non-white. In addition to air pollution variables based on county of residence, which were considered in some detail, information on individual level covariates, such as smoking, were included in the analyses. In contrast to the Six Cities and ACS II studies, all measured criteria pollutants were considered equally in the analyses. As in the Harvard Six Cities and the ACS II studies, the basic analytic tool was Cox proportional hazards regression. Four different exposures and three different mortality periods were considered, yielding a total of 12 distinct exposure and mortality period combinations. Among the pollutants, the strongest associations were seen with NO_2 and peak ozone. Of these two

pollutants, the authors reported that ozone showed the stronger association with mortality, although there was an indication of a threshold at about 0.14 ppm for ozone effects. No significant PM effect was seen with any of the various measures used (total suspended particulate (TSP), PM_{10}, sulfates, fine PM). The authors point out, however, "[i]t must be recognized that all potentially harmful pollutant species are not measured routinely and thus cannot be included in epidemiology studies of this type. For this reason, those pollutants that are included should be considered as indices of the overall urban pollution mix. Further the nature of this mix has changed significantly during the period evaluated in this study."

Updated Veterans Study (Lipfert *et al.*, 2006a, b). The first published (Lipfert et al., 2006a) update of the Veterans Cohort Study extends the mortality follow-up through 2001 and considers data on county-level traffic density as a predictor in the regression analyses. Although the update finds a positive association between fine PM and mortality in contrast to the original study, the authors report that traffic density is a better predictor of mortality than any of the ambient air quality measures, including fine PM. The investigators (Lipfert et al., 2006a) conclude:

"Traffic density is seen to be a significant and robust predictor of survival in this cohort, more so than ambient air quality, with the possible exception of ozone. Stronger effects of traffic density are seen in the counties that have ambient air quality monitoring data, which also tend to have higher levels of traffic density. These proportional-hazard modeling results indicate only modest changes in traffic-related mortality risks over time, from 1976–2001, despite the decline in regulated tailpipe emissions per vehicle since the mid1970s. This suggests that other environmental effects may be involved, such as particles from brake, tire, and road wear, traffic noise, psychological stress, and spatial gradients in socioeconomic status."

In the second part of the updated study, Lipfert et al. (2006b) investigated various sub-fractions of fine PM mass and reported stronger associations between sub-fractions of the fine PM mass and mortality than total fine PM mass and mortality. Taken together, the studies of the Veterans' cohort suggest strongly that traffic density is more strongly associated with mortality than fine PM mass, and that constituents of the fine PM mixture are important in determining its toxicity.

The CARB dismisses these studies on the grounds that they are not applicable to the general population because they were conducted in a high risk population. The CARB fails to note, however, that, on biological grounds, air pollution risks would have been expected to be higher, not lower, in this high-risk group. Thus, the finding of a small or no effect of air pollution in these studies again points to the general inconsistency of findings from epidemiological studies of air pollution.

D. Fine PM and mortality among elderly Californians (Enstrom, 2005).

The author investigated the long-term association between fine PM and total mortality in a cohort of 49,975 elderly Californians, with a mean age of 65 years in 1973. After controlling for age, gender, cigarette smoking, race, education, marital status, body mass index, occupational exposure, exercise, and diet, the author reported:

“For the initial period, 1973-1982, a small positive risk was found: RR was 1.04 (1.01-1.07) for a 10 μg/m^3 increase in $PM_{2.5}$. For the subsequent period, 19832002, this risk was no longer present: RR was 1.00 (0.98-1.02). For the entire follow-up period, RR was 1.01 (0.99-1.03). The RRs varied somewhat among major subgroups defined by sex, age, education level, smoking status, and health status. None of the subgroups that had significantly elevated RRs during 19731982 had significantly elevated RRs during 1983-2002. The RRs showed no substantial variation by county of residence during any of the three follow-up periods. Subjects in the two counties with the highest $PM_{2.5}$ levels (mean of 36.1 μg/m^3) had no greater risk of death than those in the two counties with the lowest $PM_{2.5}$ levels (mean of 13.1 μg/m^3). These epidemiologic results do not support a current relationship between fine particulate pollution and total mortality in elderly Californians, but they do not rule out a small effect, particularly before 1983.”

No co-pollutants were considered. Unlike the papers by Jerrett *et al.* and Laden *et al.* discussed above, Enstrom reports in detail his estimated relative risks associated with smoking. There is a clear and striking dose-response relationship with level of smoking, and the estimated risks are in line with the expected risks associated with smoking. Nonetheless, as in other long-term analyses of air pollution and mortality, concerns regarding the adequacy of the control of strong confounders, such as cigarette smoking, remain.

The CARB ignores this study for no good reason. Criticism of this study by Brunekreef is cited. However, in another example of unbalanced treatment of the literature, Enstrom's rather detailed and convincing rejoinder to Brunekreef's criticism is not mentioned. One strength of this study, not shared by the studies relied upon by the CARB, is that the risks associated with smoking are reported as a reality check.

E. Fine PM and cardiovascular mortality among women enrolled in the women’s health initiative (WHI)

In a recent publication, researchers at the University of Washington (Miller et al., 2007) investigated the association between exposure to air pollution and the incidence of cardiovascular events, including mortality, among over 65,000 post-menopausal women between the ages of 50 and 79 enrolled in WHI between 1994 and 1998. The women were followed up until August, 2003. As in other long-term studies of air pollution, the principal analytical tool was the Cox proportional hazards model. Although this study is billed as an air pollution study, the main focus of investigation was fine PM. Other pollutants appear to have been considered only perfunctorily. In particular, the within city analyses, which yielded the highest risks for fine PM, appear not to have been conducted for the other pollutants.

The investigators estimated risks for cardiovascular events including death, associated with fine PM pollution. They computed a between-city risk (risk associated with differences in average PM levels between cities) and also a within-city risk (risk associated with differences in fine PM levels within cities). Their overall risks (RR=1.76) and their between-city (RR=1.63) and within-city risks (RR=2.28) were considerably higher than those reported in previous studies. A few points are worth noting here. If

fine PM mass concentration is determining the risk it is difficult to see why the within-city risk is so much larger than the between-city risk. Second, the reported risks are implausibly high. For example, the within-city relative risk (associated with 10 $\mu g/m^3$ fine PM) of dying from cardiovascular disease is reported to be 2.28, as noted above. By way of comparison, the relative risk associated with smoking (which the authors do not report in this paper) in Pope et al. (2004) is 1.94 for a current smoker. In a direct examination of smoking-associated cardiovascular risks among women, Burns et al. (1996, chapter 3, table 13) reported that the relative risk of dying from coronary heart disease for a woman aged 65-69 and smoking 40 cigarettes per day is 1.86.

Thus, in this paper, the within-city risk associated with a 10 $\mu g/m^3$ increase in fine PM is larger than, and the overall risk is about the same as, the risk associated with smoking 40 cigarettes per day, findings that defy plausibility. In this study the difference in fine PM concentrations between the most polluted and least polluted cities is about 25 $\mu g/m^3$. A simple calculation based on the overall result reported in the paper then shows that a woman moving from the least polluted city to the most polluted city would increase her risk of dying from heart disease four-fold.

This very recent study adds to the general dissonance in the published epidemiological literature on air pollution. Taken together, the long-term studies of fine PM pollution and mortality do no paint a consistent and coherent picture of any association. Some studies report associations, while others do not. The reported magnitude of association varies from study to study and, in some studies such as the WHI, is too large to be biologically credible. Several studies based on the ACS cohort report findings that are simply inconsistent with biology, such as the findings of statistically significant protective effects of ozone and nitrogen dioxide on mortality in the Krewski reanalyses of the original ACS study.

The CARB fails to cite an important recent study that arrives at conclusions not consonant with its position.

The CARB report fails to cite an important study (Janes et al., 2007) providing evidence that the reported associations between fine PM and mortality could be due to confounding. The study is a nation-wide analysis of the association between fine PM and mortality co-authored by prominent members of the Johns Hopkins team involved in the National Mortality Morbidity and Air Pollution Study (NMMAPS). In this study the authors conclude that the association between fine PM and mortality described in earlier studies, including their own, could be due to inadequate control of confounding.

The paper uses a new approach to investigating confounding in air pollution studies. There have been substantial decreases in air pollution in the U.S., including fine PM pollution, in parallel with decreases in death rates. It is difficult, however, to attribute the decline in death rates to a decline in pollution because of the myriad other changes in demographics and life-style that have also occurred over the same period of time.

The authors propose a new approach to addressing this issue of confounding. They note that the association between national trends in fine PM and mortality "is likely to be confounded by slowly time-varying factors, such as changes in industrial activities and

the economy, improving health care, and large scale weather events." However, these associations at the local level are less subject to confounding and, therefore, a positive association detected at this level would be more likely to reflect a causal association between fine PM and mortality. Moreover, if fine PM pollution is causally associated with mortality, then areas of the country that have seen large declines in fine PM pollution should also see larger declines in mortality than areas of the country in which there have been more modest declines in fine PM pollution.

To test the hypothesis that declines in fine PM pollution are causally associated with declines in mortality, they use a statistical approach that decomposes the association between fine PM and mortality into a contribution at the national level and another at the local level. They analyze the association between fine PM and mortality in 113 U.S. counties over the three-year period 2000-2002, and report associations between fine PM and mortality at the national, but not the local, level, and conclude that "if the association at the national scale is set aside, there is little evidence of an association between 12month exposure to $PM_{2.5}$ and mortality." This conclusion suggests strongly that the reported associations between fine PM and mortality are not causal but can be explained by confounding. Strengths of the study include the number of counties included in the analyses, the robustness of results to sensitivity analyses, and the use of regression calibration methods to adjust for possible measurement error.

In a commentary on this study that appears in the same issue of the journal, C. Arden Pope, III and Richard T. Burnett (Pp. 424-26) discuss some of the limitations of this analysis. Pope and Burnett contend that because Janes et al. use monthly mortality counts regressed against 12-month average fine PM levels, they do not exploit the short-term variability in the pollution and mortality data. This criticism is flawed. If annual average fine PM concentrations are declining and causally related to decreases in mortality rates, it is not clear why there is not enough variability to pick up an association between annual fine PM concentrations and monthly mortality.

Pope and Burnett also suggest that with only 3 years of data the study may not have adequate statistical power. The criticism has limited validity since there is sufficient power to detect associations between fine PM and mortality trends at the national level. The Janes et al. study is well done and raises serious questions regarding the reported association between fine PM and mortality.

The CARB's discussion of uncertainty is incomplete.

In its quantitative estimates of the adverse health effects from fine PM and, in particular from diesel exhaust, the CARB fails to acknowledge the cumulative nature of the uncertainties in these estimates. Every step in the process used to estimate the health risks associated with fine PM and diesel exhaust, from estimation of emissions, to converting these using regression equations into estimates of diesel particulate concentrations, to choice of health coefficients and concentration-response functions from epidemiological studies, has a large uncertainty associated with it. These uncertainties are propagated and accumulate during the CARB's estimation of the impact of fine PM and diesel exhaust on health. In an earlier document (CARB, 2006), the CARB has acknowledged the considerable uncertainty associated with each step in

the process. It is not clear, however, that all the uncertainties are considered in the estimates derived in this report. The CARB appears to have considered only the uncertainties associated with the choice of the concentration response (CR) function. A quantitative estimation of the other components of the total uncertainty should be undertaken using Monte Carlo methods.

The CARB inappropriately uses an expert elicitation report[2] for its risk assessments

In September 2006, the EPA prepared an expert elicitation report to characterize the uncertainties in its analyses of the benefits that would be expected from a reduction in fine PM pollution. A pilot phase with 5 experts was followed by a full-blown expert elicitation with 12 experts. The results obtained in the two phases were quite different, presumably because different experts were involved. The expert elicitation report (page 1-3) states quite clearly that, in the pilot phase, "[e]xperts varied in their level of confidence that the relationship between mortality and long-term $PM_{2.5}$ changes was causal, with three experts providing probabilities of a causal relationship in the 40 to 50 percent range and two providing probabilities in the 80 to 90 percent range." Thus, in the pilot phase, 3 of 5 experts were only 40 - 50 % sure of a causal association between fine PM and mortality. In the second phase of the study, "...experts... were in general more confident in a causal relationship, less likely to incorporate thresholds, and reported higher mortality effect estimates." (Expert Elicitation Report, 2006, page ix) The EPA acknowledges that these differences could, at least partially, be due to the choice of different experts. In fact, the second panel included, in addition to epidemiologists, three toxicologists and one pulmonologist. Given that the principal task assigned to the experts was to evaluate complex epidemiological data and render expert opinions on concentration-response functions, why were toxicologists and pulmonologists invited to participate in this exercise? What expertise do they possess in the quantitative interpretation of complex epidemiological studies?

There are formal methods of meta-analyses that can be used to combine the results of multiple epidemiological studies to arrive at a single estimate of risk. The individual members of the expert elicitation panel employed their own judgment to perform a **Expanded Expert Judgment Assessment of the Concentration-Response Relationship Between $PM_{2.5}$ Exposure and Mortality. Final Report Prepared for Office of Air Planning and Standards, USEPA,** subjective ‘meta-analysis’. To then combine these subjective ‘meta-analyses’ in another subjective ‘meta-analysis’ to derive a single CR function has no basis in science.

It is important also to understand that, although the EPA attempted to select a panel of impartial experts, the goal of assembling an unbiased panel is simply not achievable. Scientists who report positive associations between air pollution and human health are more likely to be published in the field than scientists who do not. After all negative findings are rarely published and neither are grants awarded to pursue negative results. Thus the EPA selection process was biased from the start. In fact, the EPA assembled a second panel of experts (Expert Elicitation Study - Peer Review, 2006) to critique the expert elicitation report. While the panel generally commended the EPA for attempting to conduct an impartial elicitation, it acknowledged also that the attempt fell short of

achieving that goal. Members of the second panel indicated that the expert elicitation could have benefited from the inclusion of panelists who are skeptical of the link between fine PM and health impacts on humans. Members of the second panel also expressed concern that the selection process excluded scientists without readily available publications in the air pollution literature, who are more likely to be skeptical. One of the members of the second panel says (page 45 of the review), "I think that further work and a great deal of discussion is (sic) needed within the broader scientific community and among the stakeholders in air pollution risk management before EPA begins to use such elicitation results as the basis for big decisions, such as setting National Ambient Air Quality Standards (NAAQS) - with multibillion dollar implications for the US economy and similarly large implications for public health." And further, "I would not like to see EPA take this report into a federal courtroom and cite it as a principal basis for the EPA Administrator's decision in setting a NAAQS for $PM_{2.5}$." Finally, the reviewers cautioned against using a summary estimate from the range of concentration response functions provided by experts for quantitative risk assessment.

Recommendations

In its revision, the CARB should address the concerns raised in this critique. In particular, all relevant epidemiologic studies should be considered and their strengths and weaknesses discussed. Alternative interpretation of the reported findings of these studies should also be considered. Many publications discussing the primary epidemiologic studies have appeared in the peer-reviewed literature but have been ignored by the CARB. Finally, any risk assessment should be based on a proper consideration of the primary epidemiologic studies and not on the range of estimates in an expert elicitation report. The myriad sources of uncertainty, including those involved in estimating the concentration of diesel particulates, should be acknowledged and considered in the risk assessment.

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Professional Profile

Suresh Moolgavkar, M.D., Ph.D. is currently a Corporate Vice President and the Director of the Center for Epidemiology, Biostatistics and Computational Biology at Exponent, Inc., an international consulting company. Dr. Moolgavkar has more than 30 years of experience in the fields of epidemiology, biostatistics, and quantitative risk assessment. He is internationally known for his work in developing mechanistically based dose-response models for carcinogenesis, and, in particular, for the two-mutation clonal expansion model, also known as the Moolgavkar-Venzon-Knudson (MVK) model. For more than a decade, Dr. Moolgavkar has also been keenly interested in air pollution epidemiology. Since 1984, Dr. Moolgavkar has been a Full Member of the Fred Hutchinson Cancer Research Center and Professor of Epidemiology and Adjunct Professor of Biostatistics at the University of Washington in Seattle. Since 2004, he has also been Adjunct Professor of Applied Mathematics. Dr. Moolgavkar has served on the faculties of Johns Hopkins University, Indiana University, University of Pennsylvania, and Fox Chase Cancer Center. He has been a visiting scientist at the Radiation Effects Research Foundation in Hiroshima, the International Agency for Research on Cancer in Lyon, and the German Cancer Research Center in Heidelberg. Dr. Moolgavkar has served on numerous review panels and as a consultant to the National Cancer Institute, EPA, Health and Welfare, Canada, The International Agency for Research on Cancer, the California Air Resources Board, and the CIIT Centers for Health Research, among others.

Dr. Moolgavkar is the author or co-author of more than 150 papers and contributed chapters in the areas of epidemiology, biostatistics, and quantitative risk assessment, and has edited three books in these areas. He was the senior editor of a monograph, *Quantitative Estimation and Prediction of Human Cancer Risk*, published by the International Agency for Research on Cancer. He is an elected member of the American Epidemiological Society. Dr. Moolgavkar has served on the editorial board of *Genetic Epidemiology*, is currently Associate Editor for Health and Environment of *Risk Analysis—An International Journal*, and on the editorial boards of *Inhalation Toxicology* and *Biology Direct*.

Dr. Moolgavkar's research has been supported largely by grants from the National Institutes of Health, the U.S. Department of Energy, and EPA.

US EPA, Lisa Conner – Research Triangle Park, NC

Subject: Comments on ARB's PM-Mortality Draft Report
From: Conner.Lisa@epamail.epa.gov
Date: 7/11/2008 12:41 PM
To: htran@arb.ca.gov
Cc: Lamson.Amy@epamail.epa.gov

Dr. Tran,

The U.S. Environmental Protection Agency's Office of Air Quality Planning and Standards has enjoyed working with your office over the past year to describe the PM-Mortality. We are pleased to see your consideration of the findings from our recently completed expert elicitation study characterizing the uncertainties in estimates of the association between PM exposures and mortality. Several staff from EPA's Air Benefits and Cost Group have reviewed your draft report, "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California" (May 2008), and we submit the following comments.

Primarily, we have some clarifying questions regarding the methods used to calculate relative risk and the betas used in the benefits modeling program. BenMAP. In recreating the calculations found in your report, we find it difficult to determine precisely how the relative risks were calculated. It appears that the relative risks were calculated in one of two ways. One way is a simple median using the estimates directly from the EPA's expert elicitation report. As you know from our conversations over the past year, this approach would not take into account any adjustments for experts views on causality, the different functional forms provided by a few of the experts, and distributions of uncertainty surrounding the estimate. This approach also does not account for the views of a small number of the experts who offered different judgments of the concentration-response (C-R) function at low levels of ambient concentrations of PM in comparison to high concentrations. Without consideration of these issues, the draft report currently does not accurately reflect the views of the experts, or the findings by EPA. Therefore, EPA does not recommend the use of a uniform approach calculating the median of elicitation estimates to characterize PM-mortality risk. The second approach that we considered may have been employed is a more sophisticated approach that EPA's contractor, Industrial Economics, Inc. (IEc), used to adjust for the complexities mentioned above, and is shown in the analysis spreadsheet they sent to you on June 25, 2008. To summarize the information offered in the spreadsheet, IEc used a Monte Carlo technique to take 1000 random draws of each experts' elicited C-R coefficients (adjusted for causality) using their specified distribution to calculate the median, 5th percentile, and 95th percentile for a low and high concentration. IEc's method shows that a lower bound relative risk estimate of 3% is too high and varies at different ambient concentrations.

We also appreciate the responsiveness of your colleagues to our request to review the configuration file used in BenMAP, from which we were able to determine the betas for

the C-R function. It appears that the rounded relative risk estimates of 10%, 3%, and 20% were used to calculate the betas for BenMAP using the formula Beta = ln (Relative Risk) / delta PM. In addition, it is our understanding that the beta for the primary estimate was truncated to 0.01 instead of using the full estimate of 0.00953. If our understanding is correct and you did employ a truncation and a calculation of the betas using rounded relative risk estimates, this inserts unnecessary errors of approximately ± 10% into the primary mortality calculation. We recommend using the actual value of 0.00953 and employ the method below instead of rounding the relative risk values.

With respect to the method for calculating relative risk values, EPA typically shares the configuration files for BenMAP to users and would be happy to provide them to your colleagues if interested. EPA's configuration files maintain as much of the information from elicitation as is possible in that it uses the functions of each expert with their own specified coefficients, functional forms, distributions and conditional responses that are dependent on the relevant ambient concentration. Using Latin hypercube points available in BenMap, we recommend that you run your air quality grids through this configuration and calculate the median of the results, as well as the 5th percentile and 95th percentiles of the results. Although this method would take more computer processing time than the method expressed in the draft report, it would not be prohibitively time consuming, as there are only 7,000 census tracts in California. This represents only a fraction of the number of grid cells that EPA routinely uses for national analyses. We think this method would be more transparent, align more closely with the PM Expert Elicitation results, and have fewer rounding and truncation errors. Summary statements such as an approximate 10% increase in mortality for a 10 ug/m3 increase in PM could still be used, but perhaps they should not form the basis of the calculations.

Finally, on a minor note, we also noticed a typographical error in the report. The formula on page 27 has a parenthesis in the wrong place. Instead, it should read: $\Delta Y = -Yo\ [\exp(-\beta * \Delta PM) - 1] * Pop$.

Again, EPA is very glad to see your clear understanding of the data obtained from the PM-Mortality Expert Elicitation in your application to California's air quality. If you have any questions about the comments above or would like to discuss the elicitation further, please feel free to contact myself or Amy Lamson of the Air Benefits and Costs Group at (919)541-4383.

Sincerely,

Lisa Conner
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Frederick W. Lipfert, Environmental Consultant, Northport, NY

Comments on CARB's estimates of the effects of air pollution associated with port operations and goods movement on human mortality.

Frederick W. Lipfert, Ph.D
Environmental Consultant
Northport, New York
May 30, 2008

General Comments

I support CARB's efforts to quantify these transportation-related impacts, which are consistent with recent worldwide concerns about the health effects of exposure to vehicular traffic and diesel emissions. CARB's present approach is to build on an existing EPA assessment of cohort studies of long-term mortality effects of PM2.5, by attempting to convert local transportation impacts to PM2.5 by using NOx as the indicator of traffic impacts together with estimates of the ratio of diesel PM to NOx. However, as pointed out in numerous studies, the total mass of PM2.5 is not an appropriate air quality indicator for traffic impacts per se, since PM2.5 mass is dominated by secondary pollutants not directly associated with local transportation effects. Diesel PM comprises a small fraction of total PM in most locations. Data on diesel PM are available from EPA's National Air Toxics Assessment (NATA), and data on ambient elemental carbon (EC) are available from EPA's PM2.5 Speciation Trends Network (STN).

CARB used NOx data as a predictor of diesel PM and stated that most California NOx is emitted by diesel engines. A number of cohort studies (discussed below) have considered associations between NOx and mortality, and those results would have provided a more direct method of estimating the transportation-related health effects of interest.

My comments focus on the following issues:

1. Identification of the "relevant" scientific literature.
2. Exclusion of recent traffic-related and other cohort studies.
3. Mischaracterization of the Washington University-EPRI Veterans Cohort Mortality Study
4. Ramifications of using the surrogate variable PM2.5 to generate a causal dose-response function.
5. Misuse of infant mortality studies

“Relevant” Epidemiology Studies Considered by CARB

The 2006 EPA expert judgment report, as summarized by Roman et al. (2008), lists the published studies used by their “experts”; altogether, the 12 experts listed 32 citations, 29 of which are related to either the Harvard Six Cities Study or the American Cancer Society (ACS) studies (p. 19 of the CARB report). Seven of the 12 experts were directly involved in these two projects. Only one European cohort study and no Veterans Cohort papers are cited. The 2006 expert report mentions “traffic” only in passing and not as an effect modifier, and only four of the twelve experts thought PM composition to be important. Only one of them thought that the California-based AHSMOG studies are important. It thus seems abundantly clear that this expert judgment report is largely irrelevant to CARB’s task of assessing local health effects of transportation.

The question of “representativeness” of the various cohort studies was discussed in the expert report, with respect to the entire U.S. population. However, CARB should be concerned with representing the California population, which suggests that the Enstrom (2006) and AHSMOG studies should have been emphasized. If the Miller et al. (2007) study of women is included, then the Veterans Cohort studies of males should be as well, especially since this is the only cohort with appreciable numbers of non-whites. The Harvard Six Cities study is clearly irrelevant to California, even though this is the only US study with randomly selected subjects. It is difficult to understand why the ACS cohort of while middle-class volunteers should be considered “representative” of the whole US, let alone California. Further, the Krewski et al. (2000) re-analysis Pope’s 1995 ACS paper clearly showed an absence of excess mortality in California, in contrast with the AHSMOG, Enstrom, and Veterans (Lipfert et al., 2000) studies.

The CARB report lists a large number of additional references (Table 1), but seems to have overlooked salient points in several of them. Jerrett et al.’s 2005 intraurban analysis of PM2.5 gradients within the Los Angeles metropolitan area implies traffic effects, as the only logical wide-spread local emission source. The AHSMOG study of McDonnell et al. (2000) was limited to subjects living near airports, which also implies traffic effects (significant for males only). Miller et al.’s 2007 analysis of the Women’s Health Initiative found much stronger local than regional mortality risks, which also implies traffic effects. The Table 1 entry for the 2000 and 2003 Veterans Cohort Study is totally out of context with the mainly negative and significant risks reported for PM2.5 in those papers. The VA citation for 2006 does not specify which of the two 2006 papers and is also out of context with the bulk of the PM2.5 risk estimates in both of them. Enstrom (2005) finds significant PM2.5 risks for only a portion of the total follow-up period, with a strong negative temporal trend. The results of Hoek et al. (2002), Beelen et al. 2008), and Filluel et al. (2005) for black smoke do not relate to other estimates for PM2.5. Beelen et al.’s results for all-cause mortality and PM2.5 are not significant. The risk estimates of Hoek et al. (2002) and Finkelstein et al. (2004) for living near highways do not relate to PM2.5. The cystic fibrosis risk estimate of Goss et al. (2004) was greatly attenuated after controlling for lung function. While these estimates were originally published by Dockery and Pope (who is an official scientific advisor to CARB), CARB should have taken more care to assure completeness, accuracy, and conformity with the contexts of the original publications.

The MESA Cohort study listed in Table 2a (Auchincloss et al., 2008) found that

exposure to 10 μg/m3 of PM2.5 increased blood pressure by about 1 mmHg, which has little or no clinical significance. They also noted that this relationship is stronger "in the presence of high traffic exposure."

Recent Studies on Effects of Traffic Exposures

The recent epidemiological literature has a strong focus on effects of vehicular traffic that could lend support to CARB's new program of ameliorating local transportation air quality impacts. Many of these new studies have apparently been overlooked by CARB, and many of them also make the point that unspeciated PM mass air quality indicators like PM2.5 or PM10 are not helpful in this regard. Our new Veterans cohort papers were not considered, perhaps because they are new, but our 2006 report on PM2.5 constituents and related pollutants (Lipfert et al., 2006b) was also not considered by the EPA expert judgment assessment (Roman et al., 2008).

De Kok et al. (2006) conclude that "traffic intensity does not always explain local differences in PM toxicity, and these differences are not necessarily related to PM mass concentrations." Knox (2008) concluded that high 1996-2004 mortality rates in 352 English local authority areas were associated with elevated ambient pollution levels from "road transport." Medina-Ramon et al. (2008) found that "residential exposure to traffic-related air pollution increases the mortality risk after hospitalization with acute heart failure." Jerrett et al. (2007), working with the American Cancer Society CPS-II cohort, concluded that sulfate effects have declined over time and that "toxic mobile sources are now the largest contributors to PM in urban areas." Ostro et al. (2008) found "significantly higher effect estimates among those with lower educational attainment" and mentioned "motor vehicles, especially those with diesel engines." Park et al. (2008) concluded that "exposure to ambient particles, particularly from traffic" are associated with a risk factor of atherosclerosis. Morgenstern et al. (2008) found "strong positive associations" between distance to the nearest main road and asthmatic bronchitis, hay fever, eczema, and sensitisation." Peretz et al. (2008) exposed 16 young adults to high concentrations of diluted diesel exhaust (gases + PM) and found only weak, nonsignificant, effects on heart rate variability; this suggests heterogeneity in responses to traffic exposures. Sarnat et al. (2008) found relationships between cardiovascular ER visits and mobile sources of PM and biomass combustion. All of these studies and many that preceded them show the need to focus on exposures to source-specific PM constituents rather than PM mass. This requires attention to the most recent studies.

Use of the Washington University-EPRI Veterans Cohort Mortality Study

The Veterans Cohort comprises about 70,000 male military veterans recruited from 32 VA treatment centers across the nation in 1975. Distinguishing features of this cohort include individual data on blood pressure, relatively homogeneous socioeconomic status (SES), and uniform access to health care through VA hospitals. Our statistical analyses differ from those of other US cohorts in terms of using county-level air quality data and zip-code level contextual variables to capture potentially confounding factors such as income or poverty status. We use heating degree-days to account for climate factors, which may serve as a surrogate for Vitamin D through exposure to sunlight, a

factor that that has been recently emphasized in the press (Autier and Gandini, 2007; Mead, 2008). We analyze survival in terms of 5-8 yr subsets of the overall 26-y follow-up period, in order to allow the Cox proportional hazards model to adjust for possible temporal changes in confounding factors after enrollment in the cohort.

I appreciate CARB's citing of most of the publications on this cohort; three additional forthcoming papers are listed below (Lipfert and Wyzga, 2008; Lipfert et al., 2008a,b). However, CARB's reliance on the 2006 EPA report on PM2.5 mortality studies imposes a severe restriction on the validity of their analysis, given the large number of important and relevant studies that have since been published, including the new results for the Veterans Study. EPA commissioned that early assessment effort to support their decision to regulate PM2.5; CARB's stated objectives for this assessment are entirely different and they should create their own literature database for that purpose.

The initial Veterans Cohort paper (Lipfert et al., 2000a) was greeted with some skepticism, since we showed that including contextual variables like climate and neighborhood poverty status in the Cox proportional hazards model greatly attenuated the estimated mortality risks associated with sulfates and PM2.5. This finding has since been confirmed by Jerrett et al (2005). Some skeptics attributed our results to effects of increased blood pressure that might have been caused by air pollution exposure, thus providing a pathway for effect modification. Our 2003 paper laid that claim to rest, by showing that air pollution risks were not modified by hypertension status. CARB now finds our cohort to be "unrepresentative" of the general population and thus dismissed all of our findings. As shown below, this claim is also without merit. Although our cohort represents a group of slightly lower-than-average socioeconomic status (SES), comprising about 90% enlisted military personnel, its other characteristics are not atypical for that group, circa 1975 (the period of cohort enrollment):

Characteristic	Veterans Cohort	U.S. population (data source)
race (% black)	35%	18% of those with low education (1)
blood pressure (mean systolic)	148 mmHg	139 mmHg (2)
current smokers	57%	41% (3)
ever smokers	81%	78% (3)
body mass index	26.3	26.7 (4)

data sources:
(1) Meara ER, Richards S, Cutler DM, *Health Affairs* 27:350-60 (2008)
(2) Drizd T, *Vital and Health Statistics* 11, No. 234, Public Health Service, Washington, DC. 1986
(3) Smoking and Health, a report of the Surgeon General, U.S. Government Printing Office, Washington, DC 1979
(4) Jackson AS, Stanforth PR, Gagnon J et al., *Int J Obes Relat Metab Disord* 26:789-96 (2002).

The question of race deserves further discussion. According to 2006 Census estimates, the population of Los Angeles County is only 29% non-Hispanic white, and blacks comprise about 25% of all non-Hispanics. These figures are 41% and 14% for the whole state, but the transportation air quality problem is centered in LA County. Only the Veterans Cohort study includes an appreciable fraction of African-American subjects; this fact alone demands that our findings be considered when making mortality risk estimates for a non-white population. Further, the male gender, lower SES, higher blood pressures, and larger fractions of smokers places the Veterans Cohort in the category of a "susceptible subpopulation", for which several studies have shown that air pollution health effects are expected to be more, not less, severe.

CARB states that the risk estimates for PM2.5 published for the Veterans Cohort are "unstable". This suggests that CARB has selected studies for consideration on the basis of outcomes and not from first principles such as study design. In fact, our estimates are quite self-consistent when their details are considered, such as the source of the PM2.5 data. The 1979-84 IPN PM2.5 data from Lipfert et al. (1988), which were also used by Pope et al. in the American Cancer Society papers, have much less geographic coverage than the 1999 and later EPA PM2.5 data. This discrepancy can affect the risk estimates because different cities are involved. Second, there are temporal trends in the risk estimates, in part because of the long follow-up period and potential temporal changes in the confounding risk factors. Finally, the model structure must be considered, whether other pollutants are considered jointly and whether the cohort has been stratified to consider effect modification or expanded because of additional mortality follow-up.

Table 4 in Lipfert et al. (2003) compares mortality risks estimated for the 1979-81 IPN data for three mortality follow-up periods, with and without stratification by blood pressure. Data from the 2000 paper are also shown there for reference. Eight of these 9 estimates are negative, some significantly so. They indicate a ~10% drop in mortality for a 10 $\mu g/m^3$ increase in PM2.5, with risks becoming more negative with more recent mortality periods. Stratification by blood pressure had little consistent effect. All of these estimates are reasonably self-consistent.

The 2006 Veterans Cohort papers use 1999-2001 PM2.5 data from EPA's national network, with the mortality follow-up period extended through 2001. Table 3 in Lipfert et al. (2006a) shows a 6% increase in 1997-2001 mortality for an increase in PM2.5 of 10 $\mu g/m^3$ that is not significant. Table 4 in Lipfert et al. (2006b) shows a significant increase in 1989-96 mortality of 15% for an increase of 10 $\mu g/m^3$. However, 1997-2001 mortality risks were lower and not significant (Table 5) at 2.6% per 10 $\mu g/m^3$ (based on a restricted set of subjects who lived in counties having ambient NO2 data). These estimates are also self-consistent and indicate a decreasing trend in the effect of PM2.5 on all-cause mortality.

Tables 4 and 5 in Lipfert et al. (2006b) also show the results of regressing traffic density and PM2.5 jointly. In both cases, traffic density remains significant and accounts for almost all of the combined air pollution risk. This is further evidence that PM2.5 is only a surrogate for traffic impacts. Table 3 in Lipfert et al. (2006a) also shows

29 pollutants ranked in decreasing order of “achievable” effect (risks based on the difference between mean and minimum concentration levels). After traffic density, elemental carbon (EC, significant), NO2, and nitrate (significant) are all more important than either PM2.5 or PM10, which have similar effects. Vanadium, peak ozone, and nickel rank slightly lower than PM. Table 4 in that paper shows results for two-pollutant models, in which traffic density and EC tend to prevail. We have found similar results in a new paper (submitted in 2008) based on modeled estimates of exposures to a wide range of air toxics and traffic pollutants, for each county in the US. We continue to find negative effects of sulfate, based on both measured and modeled exposure estimates. The Veterans Study is the only cohort study to have considered the long-term effects of PM2.5 constituents and air toxics in detail, in conjunction with the usual criteria air pollutants.

CARB uses NOx as an index of traffic effects as part of their methodology of applying mortality risks based on PM2.5 to local traffic effects. The Veterans Cohort study has reported important mortality risks based on ambient NO2 or NOx in most of its publications. These values represent the fraction of all-cause mortality associated with mean ambient concentrations, and are quite self consistent:

Lipfert et al., 2000: 0.045 with contextual variables in the model: 0.075 without these variables.
Lipfert et al., 2006a: 0.053 for 1989-96 mortality; 0.108 for high-density counties in 1997-2001.
Lipfert et al., 2006b: 0.086 for NO2, 0.077 for the nitrate content of PM2.5
Lipfert et al., 2008b: 0.074 for NOx in all counties; 0.167 for NOx in high-density counties.

Other cohort studies have reported significant NO2 mortality risks in Europe, but Pope et al. (2002) found no NO2 effects for the ACS cohort, perhaps because their averaging of ambient air quality over multi-county SMSAs obscured such local effects.

Identification of Response Thresholds

PM2.5 is defined on the basis of a measurement method and comprises a variable mixture of many different types of particles, some of which may be more toxic than others. For example, sulfates and nitrates have largely been exonerated at current ambient levels (see Schlesinger and Cassee [2003], for example), while certain metals and organic compounds (including diesel particulate) may be of concern. PM2.5 (mass) is thus primarily an indicator or surrogate variable for whatever toxic compounds may be included; its use in epidemiology induces measurement error with respect to the true agents of harm. Such measurement errors may bias the slopes of dose-response functions towards the null (Mallick et al., 2002), but they also obscure any thresholds that may be present (Lipfert, 1999; Kuchenhoff and Carroll, 1997). Thus, failure to find a mortality threshold for PM2.5 is to be expected because of its surrogate status and does not imply that traffic-related exposures are toxic at all concentration levels. Lipfert and Wyzga (2008) and Lipfert et al. (2008a,b) show that thresholds in traffic effects may exist at around 4000 vehicles per day, as a county-wide average. This also extends to NOx and specific transportation-related air toxics like benzene or formaldehyde, but not

to diesel PM (Lipfert et al. 2008b). Our most recent Veterans Cohort paper (Lipfert et al., 2008b) also shows that these more specific traffic-related air toxics imply stronger risk estimates than traffic density (which is clearly a surrogate variable), which is in turn a better predictor than PM2.5.

The CARB report cites a paper on measurement error that is specifically based on the Harvard Six Cities Study (Mallick et al., 2002). However, this paper deals only with bias in the regression coefficients (slopes) and does not touch upon the more important problems of dose-response function linearity, thresholds, or competition in multiple-pollutant models. Thus, the measurement error issue remains and applies to health studies that use surrogate predictor variables like PM2.5.

Infant Mortality Studies

CARB selected infant mortality studies by Woodruff et al. as part of their assessment of transportation-related health effects. These studies clearly indicate PM10 rather than PM2.5 as the best predictor. Lipfert et al. (2000b) showed that the relationship of Woodruff et al. (1997) was dominated by high mortality rates in sparsely populated areas in the Western US, where access to medical care may have been issue and PM10 may be unduly influenced by windblown dust. Lipfert et al. (2000b) also showed sulfate aerosol, a major constituent of PM2.5, to have a significant *negative* relationship with infant mortality. This may be a reason that Woodruff et al. (2008) find stronger infant mortality effects with PM10 than with PM2.5. Kaiser et al. (2004) found a relationship with PM10. Further, Green et al. (2004) note that non-white children are more likely to attend schools located close to freeways in California, suggesting differential population exposures to traffic by race. Brauer et al. (2008) found that residence within 50 m of a highway to be strongly associated with low birthweight in Vancouver. None of these studies implicate PM2.5 with respect to infant health.

Concluding Comments

California has long been a national pace-setter in environmental protection and air pollution abatement. I urge CARB to take this opportunity to depart from the outmoded use of regulatory air quality indicators like PM mass and to make full use of the new information on specific toxic compounds that is increasingly available. Because of the economic impacts of the proposed transportation regulations, scientific credibility is important and will be enhanced by making full use of the latest and most specific information on exposures and health effects.

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July 11, 2008

Dr. Hien Tran
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Air Resources Board
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Dear Dr. Tran:

On behalf of the Health Effects Institute, I am pleased to provide these comments on the Air Resources Board's Draft *Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California* (May 22, 2008). As you know, HEI has supported a number of the key epidemiologic studies that ARB and others have available to apply in such analyses and we welcome the opportunity to share our perspective on how these studies and others were used in your effort.

The estimation of such public health impacts, particularly in the light of continually evolving science, is an important undertaking, and we applaud ARB's efforts to do this in a transparent and thoughtful manner. We were particularly impressed by four aspects of the analysis:

- The generally thoughtful review of the existing PM literature that is relevant to the question, and of the degree to which such studies are relevant to California,
- The clear explanations of the methodologies chosen and how they were applied,
- The effort to conduct a number of sensitivity analyses to test the validity of the central analysis; and
- Inclusion of an explicit discussion of limitations and uncertainties.

Overall, we concur that the current science is sufficiently robust to estimate the effects of exposure to fine particles on premature mortality, and that given the nature of the results, that the public health implications of any such estimates are likely to be of importance.
At the same time, we did note several areas where the analysis could be better accomplished and have some suggestions that we hope could enhance your efforts going forward. These include:

- Comments on several specific studies discussed;

- The expert elicitation process and suggestions for broadening the sensitivity analysis, and
- Questions about the new method proposed for estimating exposure to diesel PM.

The Studies Considered In general, the review of the existing studies of PM and mortality is comprehensive and well done. We do however have comments on two of these studies which have been supported by HEI: The Jerrett Study (2005) This well done study was funded by HEI as one part of a series of extended analyses being undertaken by a team led by Dan Krewski of the University of Ottawa. The higher levels of relative risk found in this analysis (when compared to the broader ACS analysis) are intriguing, and raise the possibility that better estimation of exposure as was attempted in this study could reduce exposure measurement error and result in a "truer" estimate of risk. To test that however, the investigators also attempted a similar analysis in the New York Metropolitan Area which has recently completed HEI Peer Review, was presented at the HEI annual conference, and is now going "into press" at HEI. As illustrated in Table 1 below, this analysis did not find a similarly elevated relative risk. Although there are notable differences between the two settings and the analyses, the New York analysis raises the question going forward about how best to generalize from

	LA		NYC
Cause of Death Cox Model Covariates	LUR	Kriging	LUR
All Causes			
PM2.5 only	1.20 (1.08,1.32)	1.24 (1.11,1.37)	1.01 (0.94,1.05)
44 Individual Covariates	1.14 (1.03,1.27)	1.17 (1.05, 1.30)	0.98 (0.95,1.02)
IHD			
PM2.5 only	1.42 (1.15,1.74)	1.49 (1.20, 1.85)	1.11 (1.04,1.18)
44 Individual Covariates	1.33 (1.08,1.63)	1.39 (1.12, 1.73)	1.07 (1.00,1.15)
Cardiopulmonary			
PM2.5 only	1.18 (1.02,1.36)	1.20 (1.04, 1.39)	0.98 (0.93,1.03)
44 Individual Covariates	1.11 (0.97,1.28)	1.12 (0.97, 1.30)	0.95 (0.90,1.01)
Lung Cancer			
PM2.5 only	1.46(1.01,2.10)	1.60 (1.09, 2.33)	1.04 (0.91,1.18)
44 Individual Covariates	1.39(0.96,2.01)	1.44 (0.98, 2.11)	0.96 (0.84,1.09)

Table 1. Relative Risk of PM2.5 Mortality per 10µg/m3; Results for New York and Los Angeles

the Jerrett results and calls for attempts to do additional such analyses in different geographic settings and scales. To this end, we were pleased to learn recently that ARB has moved forward with funding these investigators to perform a broader California analysis in the ACS dataset, and we are looking forward to seeing those results as they develop.

The Hoek (2002) and Beehlen (2008) Studies Although these two studies in a Dutch nutrition cohort were not as central to either the expert elicitation or your analysis, there is an important misrepresentation of the Beehlen study results in your document that should be remedied. This study was funded by HEI and involved analyses in the full

cohort. We agree that the investigators did find associations with PM and traffic exposure and mortality. However, the statement on P. 8 that the Beehlen study "reinforces the conclusions of the pilot study" is significantly overstated. The effect estimates in the full cohort were substantially smaller than in the pilot study, and the traffic related effects were no longer substantially larger than the PM effects (as they had been in the pilot). In the full HEI report which is now in press, the investigators do an excellent job of exploring why these results have changed so substantially. We would suggest that ARB revise this text and more carefully describe the differences in the results between the two.

Expert Elicitation and Suggestions for Sensitivity Analysis As you note in the document, EPA went to substantial lengths to develop their expert elicitation process, and HEI assisted them in this effort when it became apparent that toxicological, biological and medical experts were underrepresented and we were asked to nominate capable individuals for that purpose. Probably more than anything else, the value of a formal expert elicitation process is that it makes explicit the assumptions and judgments that all experts normally make, and thus allows a more transparent assessment of how a particular risk estimate has been obtained. Your report does a good job of presenting the process and results from EPA in that transparent way.

Having said that, the formal process of expert elicitation is still being developed, and we would like to first call ARB's attention to a current peer review being undertaken by the US EPA Science Advisory Board of the use of EPA's expert elicitation in its own benefits assessment for PM2.5. That review is expected to conclude shortly, and may help inform your revision of the current document.

We would also note that expert elicitation is inevitably a "snapshot in time" of the science then available and to be reflective of the current state of the art must be revisited on a fairly regular basis. For example, at the time of the EPA process, the Jerrett results were available – and played a significant role in a number of the experts' judgments - but not those for New York (which as we note above are significantly different and lower). Similarly the Beehlen study was not then available (although the Hoek study appeared to have not played as large a role (perhaps because it was understood to be a pilot study).

Although no one analysis can include every new study, the continually evolving literature requires, therefore, even more attention to sensitivity analysis than your substantial existing work by exploring a fuller range of possible outcomes other than your adopted approach. In this context, it appears that in all of your sensitivity analyses you have chosen to test your approach against various permutations of combining only three studies, two of which – Jerrett and Pope – overlap. We would suggest therefore that you explore a wider range permutations, including for example both the original Harvard Six Cities and the Laden study in different analyses (since the original study appeared to have had a greater influence on the elicitation than the Laden study) and conducting more of the analyses without the Jerrett results (given their overlap with ACS and the fact that the New York results suggest that they will need to be replicated further to fully understand how robust they are). We can also of course make available the New York ACS results that are now entering "in press" status.

The New Method for Estimating Diesel PM Exposure As you know, despite many efforts by a range of experts, we have not yet identified one particularly useful marker (or set of markers) to represent the level of diesel particulate matter in the air (cf. HEI's Communication 10, *Improving Estimates of Diesel and Other Emissions for Epidemiologic Studies*, 2003). In this context, it is useful to continually attempt to develop and test new methods and we appreciate that that is what ARB is attempting to do as one part of this document. However, the issues around the development of such a metric (in this case using NOx), are not insignificant, and quite separate from the important set of methodologic issues that you are addressing on health impact estimation for PM generally in the rest of this document. They seem deserving of their own review, vetting, and publication in the broader literature before being incorporated into a document like this. HEI – given its long standing interest and expertise in this area - would be pleased to assist ARB in that process.

We appreciate the opportunity to make these comments and would be pleased to provide additional information and/or respond to questions you might have.

Dan Greenbaum President

Industrial economics incorporated, Cambridge, MA

July 11, 2008

Industrial Economics, Incorporated (IEc) Comments on "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California," (May 22, 2008 Draft)

Industrial Economics, Incorporated (IEc) is pleased to have the opportunity to review the May 22, 2008 draft California Air Resources Board (CARB) Staff Report, "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California." IEc, a consulting firm based in Cambridge, Massachusetts, is the lead consultant and author of the U.S. EPA-sponsored expert elicitation (EE) studies of the mortality impacts of PM2.5, the results of which serve as critical inputs for CARB's analysis. IEc is providing the following editorial comments on the CARB report, presented in the order they appear in the document, to help clarify the descriptions of the methods and results of the expert elicitation study. Questions regarding these comments should be directed to Henry Roman of IEc (hroman@indecon.com).

- General comment: Please cite the Industrial Economics, or IEc, reports for the 2004 pilot study and 2006 study as (IEc, 2004) and (IEc, 2006).

- Page 10, second to last paragraph – please change "we adapt a report" to "we quote extensively from a report"; also please use quotes or a block quote format to indicate direct quotes from the IEc report.

- Page 10, last paragraph – the use of the phrase "convened a panel of twelve experts" suggests that EPA directly selected the panel of experts. To avoid confusion, we recommend changing the sentence to read: "As a result, U.S. EPA conducted an expert elicitation study with twelve experts…" We also recommend revising the rest of this sentence to more accurately describe the objective of the expert elicitation study. Please change "…to assess the reduction in premature death in the adult U.S. population…" to "…to better characterize uncertainty in the estimated reductions in premature death in the adult U.S. population…"

- Page 10, last paragraph – the use of the phrase "results from the panel's report" suggests that the experts themselves wrote the report. We suggest replacing this with "results from the U.S. EPA-sponsored expert elicitation study."

- Page 10, last paragraph, last sentence – "In their assessment" implies that the experts collaborated to produce a consensus opinion, which is not the

case. Also, experts were not restricted to published literature only. We recommend changing the text to say, "Each expert in the elicitation study considered relevant theoretical and empirical evidence available at the time of the study. Experts were encouraged to consider evidence that both supported and cast doubt on a PM2.5-mortality relationship."

- Page 17, third bullet – we recommend moving the last sentence of this bullet to the end of the previous bullet. The second bullet discusses the experts' views on threshold and the text about Expert K's threshold seems to fit best here.

- Page 23 and 24 – please provide more detail about the process CARB used to develop the median estimates for the 5th, 50th and 95th percentile for the PM-mortality relationship, including how CARB dealt with the issue of addressing the distributions that are conditional on a causal relationship and the distributions that vary with PM2.5 concentrations.

- Page 23, last paragraph – The calibration question approach described here is not universally endorsed by EE practitioners and is controversial, in part because it is not clear how well the calibration questions truly measure expertise in the field of interest. The fact that many EE applications use calibration is more a reflection of the prolific nature of those who support calibration, rather than an indication of wide acceptance of the approach. We recommend changing the sentence starting "Many expert elicitation applications use a series of calibration exercises.." to say "Some expert elicitation practitioners use a series of calibration exercises…". Later in that same sentence, please change "determine the ability of experts" to "assess the ability of experts". "Determine" implies a greater level of accuracy for the calibration exercises than is warranted.

- Page 24, 2nd full paragraph, 1st sentence: "Simple averaging of experts' distributions can be used to corroborate the above assessments…" We do not understand this statement. Recommend deleting this part of the sentence.

- Page 27, 3rd full paragraph – Change "census track" to "census tract" (2 occurrences).

- Page 28, 3rd paragraph ("Cut-Off Level of 7 ug/m3). We recommend deleting the first sentence ("As discussed above…"). The results of the elicitation study do not provide support for a threshold at 7 ug/m3, as this sentence implies. Furthermore, this sentence could be interpreted to mean that the expert who provided a different C-R slope below 7 ug/m3 supported a threshold, which he did not.

John Dale Dunn, Carl R. Darnall Army Medical Center, Ft. Hood, TX

John Dale Dunn MD JD
Civilian Faculty, Emergency Medicine,
Carl R. Darnall Army Medical Center, Fort Hood, Texas

June 23, 2008

Addressed to the California Air Resources Board (CARB) and
Interested Elected and Appointed Officials.

Comments on the CARB Diesel and Small Particles research and policy making. Critique of "Estimating premature deaths from small particulates and diesel fumes in California."

Draft Report from CARB Staff and Engaged Experts, May 22, 2008

My opinions expressed here are not opinions of the Department of Defense or the Army.

Biographical information

I am a 36 year physician and 29 year inactive attorney. I teach Emergency Medicine at Carl R. Darnall Army Medical Center, Fort Hood, Texas, so I have general and specific knowledge of toxicological science. I was a 10 + year public health authority, and a lecturer and writer on environmental law and regulation for the past 18 years.

I have expertise in public health epidemiological research and principles and public policy issues that pertain to air pollution and other environmental policy matters.

I am familiar with the rules of evidence and the standards for admissibility of scientific evidence under the new *Daubert v. Merrill Dow* dicta and the *Reference Manual on Scientific Evidence* 2nd Edition, published by the U.S. Federal Judicial Center.

I am a policy advisor for the Heartland Institute of Chicago, and the American Council on Science and Health of New York City. In the past I have submitted memoranda and argued to the EPA, and it's Board of Scientific Counselors on the problems of EPA distorted and weak toxicological and epidemiological health effects science.

I will focus here in my comments on science issues that impact CARB regulatory actions and policy making on diesel and small particles.

I submit that:

1. The studies on air pollution listed in the report as key studies and relied on by CARB and its experts propose death data that do not meet the requirement for proof of anything. The studies listed fail to meet the requirement of a relative risk of at least 2 for observational studies. The researchers who promote and rely on such studies have decided not to even attempt to explain or excuse such nonsense
2. The other alternative science proposal being foisted on the public by CARB is that the death studies that assert acute deaths can propose a short period lag time for death from air pollution. That is nonsense, and Dr. Utell, a physician expert on the CARB panel, a critical care physician, knows it. Sudden death from cardiac arrhythmia is not in play here, and Dr. Utell or any reasonably competent physician could keep a person with end stage lung disease alive for an indefinite period. People don't drop dead in the streets from dust or diesel. Studies that propose short lag times are preposterous.
3. The CARB research ignores that null effect of the Enstrom study which is specific for Californians, and the null effect shown in the later half of the Pope ACS study. Those two studies, when combined with the null Western U.S. and California effect of the Krewski map, create evidence that cannot be ignored by the CARB.
4. Studies that falsify a scientific assertion are more pertinent to the scientific inquiry than studies that support a proposition, since the goal of science is to avoid a type one (false positive) error.

Intrusive regulatory regimes should only be enacted if the research is conclusive that a human health problem exists. California air quality does not justify the crisis tone or aggressive policy attitude of the CARB.

CARB is faced with the problems that make aggressive regulatory approaches appear to be a desperate maneuver to promote panic mongering. CARB should consider the following:

1. A major study by the Health Effects Institute shows no excess mortality from fine particles.
2. The Enstrom Study of a robust cohort of Californians studied over a significant period of time shows no death effect from small particles.
3. The US EPA 2002 report of diesel exhaust health effects showed no effect.
4. The previously mentioned Pope second half data and the Krewski map of effects shows that California residents are not suffering any adverse effects from air pollution.

<u>LEGAL STANDARDS FOR EVIDENCE WILL DELEGITIMIZE THE CARB STUDIES AND PUT FUTURE CARB POLICY POSITIONS AND LITIGATION AT RISK</u>

The Federal Judicial Center, in its *Reference Manual on Scientific Evidence,* 2nd

edition outlines advice for determining admissibility of scientific evidence in Federal Courts, and advises Federal Judges and Lawyers practicing in Federal Courts to adhere to that advice in complying with the Rules of Evidence. .

An electronic version of the *Reference Manual* can be downloaded from the Federal Judicial Center's site on the World Wide Web.
http://air.f jc.gov/public/f jcweb.nsf/pages/16
For the Judicial Center's homepage on the Web, go to **http://www.fjc.gov**

RELATIVE RISK AS PROOF OF CAUSATION

All the studies that are cited by CARB as key to the diesel and small particulates rules and regulatory policy violate basic epidemiology rules for proof of health effects. They all have an effect of a relative risk of less than 2 (100% increase in effect), too weak to consider proof.

In the Chapter on Epidemiology the authors, including Leon Gordis, MD Dr. P.H. the renowned former Chair of Epidemiology at Johns Hopkins School of Public Health and D Michal Freedman J.D. Ph.D. MPH from the National Cancer Institute, advise the following at page 384:

> The threshold for concluding that an agent was more likely than not the cause of an individual's disease is a relative risk greater than 2.0. Recall that a relative risk of 1.0 means that the agent has no effect on the incidence of disease.
> When the relative risk reaches 2.0, the agent is responsible for an equal number of cases of disease as all other background causes. Thus, a relative risk of 2.0 (with certain qualifications noted below) implies a 50% likelihood that an exposed individual's disease was caused by the agent.
> A relative risk greater than 2.0 would permit an inference that an individual plaintiff's disease was more likely than not caused by the implicated agent.

The studies relied on by the CARB to project estimates of deaths in California all have health effects or death effect below a relative risk of 2, again insignificant for evidence of proof of real effect.

IF CARB HAD TO DEFEND IT'S ACTIONS IN COURT OR IN AN ADMINISTRATIVE HEARING.

A careful and thorough Judge, a Judge not influenced by the environmental fanaticism so fashionable today, following the advice and guidance of the *Reference Manual on Scientific Evidence* would suggest to CARB:

1. That the CARB Key studies are weak and faulty in failing to meet the rule on relative risk.
2. That the plausibility for deaths at a few days from exposure to ambient increases in air pollution fails to meet the rules of toxicology in the *Manual.*

3. That the Enstrom study and the second half of the Pope ACS study as well as the Krewski geographic analysis map appear to falsify the CARB assertion that diesel and small particles are killing thousands of Californians every year.

A reasonable and thorough Judge would insist that CARB and its sponsored and well paid consultants and researchers explain the studies that falsify the CARB assertions and the relative weakness of the studies that rely on small effects and minimal relative risks.

Whenever a study from a reputable scientist disproves a theory or a premise, the study must be dealt with, not ignored, lest politics and intellectual fascism become the fashion, even in a bastion of free speech, the great State of California.

OTHER PROBLEMS WITH OBSERVATIONAL STUDIES USED BY CARB.

Observational studies are notoriously unreliable and uncertain, since there is no way to eliminate the more than 40 confounders that may produce error. If a study is observational rather than randomized and controlled, blinded and crossed over, there are significant problems with reliability. Reports from observational studies do not reproduce well when converted to randomized, controlled studies.

The CARB exercise of engaging multiple experts, who have relied on small effects observational studies throughout their careers, creates a mad cycle. Most of the experts engaged are included in the company of individuals who publish observational studies with relative risks of less than 2. Most have done and stand by studies that violate this basic rule of relative risk, the equivalent of the fox in the henhouse.

So consider all the CARB studies which are invariably studies based on health effects of monitored outside ambient air when humans live indoors more than 75 % of the time, particularly when they are frail and approaching death. The studies then either do long term death comparisons to air monitor data, to smooth out the effect of air pollution--or they do something more outrageous—argue that air pollution causes acute toxicity that kills within days. Neither methodology can pass the smell test.

Study methodologies and bigger computers cannot and will not be able to eliminate important confounders in observational studies, or the problem that biological implausibility of the minor current ambient air pollution causing acute deaths or chronic illness. The human organism is much more resilient and resistant than proposed by CARB or the CARB studies.

<u>Piling up “experts” who have authored these weak studies is not the answer to the question. Following the rules and looking at the studies that refute the assertions of the studies that claim death effects and health effects is the</u>

scientific way to address the question.

The proper answer is that the science is not settled, there are too many studies that show no effect, and the small effects and small relative risks are proof of nothing in the context of observational studies. CARB should be cautious.

TIME AND GEOGRAPHIC CONSIDERATIONS ARE ESSENTIAL TO GOOD ANALYSIS, AND CARB IGNORES THE KREWSKI, POPE AND ENSTROM NULL EFFECTS.

There are two good examples in the studies relied on by CARB that show that ignoring time and geography may create unreliable analysis.

The first is the study by James Enstrom Ph.D., MPH (Inhalation Toxicology 2005), referenced in the draft report on page 18, a robust and long term study of California residents, that concludes there is no death effect from small particulates in the levels found in California air.

The second is the second half of the Pope ACS study and the Krewski map to determine the implications of the null effect. When one removes the effect of the first half of the Pope ACS study, the later half of the study would show essentially no health effect in California from small particles. Pope's second half data results confirm the Enstrom study. Now CARB has two elephants in the room.

The Krewski map and the Health Effects Institute study of 2000 put a third and fourth elephant in the CARB conference room.

FALSIFIABILITY AND THE DANGERS OF "CONSENSUS"

Karl Popper, the most highly respected philosopher of science of the 20th Century, was favorably referenced by Justice Blackmun in the *Daubert v Merrill Dow* Opinion, [509 U.S. 579 (1993)] that changed the rules for scientific evidence in United States courts. *Daubert a*ssigned the role of scientific evidence and testimony gatekeeper to the presiding judge, in order to reduce the chance of junk science in the court room. In 1994 the first edition of the *Reference Manual* was published by the Judicial Center to educate judges on their role of assessing scientific evidence and testimony for reliability.

That is even though the CARB is willing to ignore the small relative risk and small effects shown by all the studies that the CARB report considers "key."

The Popper falsifiability test essentially means that a pile of studies supporting a premise is trumped by one good study that disproves the premise. Falsifiability is a key to preventing "consensus" fallacious thinking in science. CARB and its experts are victims of the consensus and refuse to recognize the elephants in the room, the studies that say FALSE.

Dr. Enstrom should be given the courtesy of an invitation to sit with the CARB

staff and consultants and review his data set and the data sets of all the key studies. Moreover, the Pope ACS study should be dissected for the second half data, and the Krewski map should be better studied on the question of California effects.

THE CARB PREMATURE DEATH NUMBERS—COMPUTER MAGIC?

As a physician I am not impressed at all by the observational studies relied on by CARB. Death certificate matching to air pollution monitor information is an invitation to data dredging. Death certificate associations with air pollution? A few micro grams of dust per cubic meter of air kills?? This data exercise appears to be number crunchers with computer power doing the association game, ignoring biological plausibility.

In 36 years as an emergency physician and family practitioner, I have not seen anyone die of small particle or diesel fume toxicity. At best these irritants might cause some decline in lung function or health, but death?

Sudden deaths from dust? See the CARB report at pages 34-38 for small particles and diesel deaths and imagine thousands of people dying every year on the streets or in the yards and fields of California. The CARB projections are an exotic numbers game done by uploading data and making associations and projections with the hard drive humming and fingers crossed. The real world is not on a hard drive and real people die in hospitals and emergency departments, not on or in computer boxes on the desks of epidemiologists who never owned a stethoscope.

People die over a long period of time from lung and cardiac ailments, as a general rule, with a few acute deaths, not caused by air pollution. Recent efforts by the radical element of the environmental medical fanatics to argue in journals that inflammatory mediators kill people in the streets, caused by exposure to some benign and minor exposure to ambient air pollution are fantastic and delusional.

Any physician, familiar with the nature of lung and cardiac disease and the tenuous relationship that can be constructed with dust-death has to smile that fanatics would be willing to compromise their scientific backgrounds to make arguments for such preposterous theories. It is silly for CARB and all its horsemen to claim that 10 or 20 thousand people will die prematurely in California every year from minor air pollution levels measured in millionths of a gram per cubic meter of air or predict that removal of a few micrograms from the air will save lives.

AN EXAMPLE OF IRRESPONSIBLE CARB SPONSORED RESEARCH

W. James Gauderman of the University of Southern California, and the Children's Health Study (CHS) which is regularly and generously supported by CARB and other governmental agencies, wrote in the January 26, 2007 issue of

Lancet about traffic air pollution effects on adolescents (*Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study*) asserting that they find a "significant" deleterious affect proportionate to residential proximity for four groups living up to and beyond 1500 meters from busy roadways. Sponsoring funding was from CARB, the U.S. EPA, and the National Institute of Environmental Health Sciences (a Subdivision of NIH). CHS has always enjoyed generous government funding.

This study was low power with a high drop out rate (3677 to 1497). The authors claimed “significant” health effects results when the pulmonary function test (PFT) results were 2% less than predicted for the more than 1500 meter group and the rest of the group results were clustered with no trend line. Any clinician knows that pulmonary function tests are imprecise and that there is a 10 % range for results. Pulmonary function studies are dependent on operator but also affected by subject effort.

The tables in the study showed a cluster of results in the groups with no trend, but there was a 93% of expected outlier result in the mid-expiratory flow for the group at less than 500 meters. That is not a trend. There is no trend. Two points can make a slope, but do not define a trend.

Most telling, however, is that the CHS study was chasing a phantom air pollution menace. Yifang Zhu’s group from University of Southern California that included a faculty member from Gauderman’s University of Southern California (Kim), published in 2002, five years before, that air pollution from busy roadways rapidly decreases at 150 meters <u>until it becomes background at slightly more than 300 meters</u> (Zhu references, 1,2,3 in the appendix). The CHS group is studying what health effects from what pollution?

In summary, this University of Southern California prominent children’s air pollution study group claims the following:

1. Pollution effects children who lived beyond the pollution from thoroughfares and highways.
2. A health effect or toxicity trend line created by one outlier and a cluster of other pulmonary function results.
3. Proof of an adverse health effect by results from pulmonary function testing that are less than the range of sensitivity and specificity for tests performed.

Although the CHS group may defend themselves as passing the peer review test for publication, that brings me back home to my original point about the CARB chosen “experts” who do and support the same kinds of research as that done by the CHS group because that is what they do—they do epidemiology in search of air pollution health effects.

Isn’t it remarkable that at this point, after 20 years of improved air quality in America and California, the CARB and its sponsored researchers are still trying

to scare the public about air quality? Claiming that thousands will die if something isn't done immediately.

Forget the slipshod methodology of this study, the questionable findings, the unnecessary scare tactics promoted by the media that publicizes the study. Ignore the economic consequences of any new regulation based on the study, move the policy agenda of the CARB forward, make the world spic and span, eliminate dust and pollutants at any cost. Breathtaking what CARB will do to control the discussion and the research it will fund and sponsor.

CONCLUSION

I challenge CARB to overturn or refute the findings of James Enstrom, the Pope/ACS second half results, the Health Effects 2000 study, and the Krewski map, all of which show no reason for aggressive California air regulations. I challenge the CARB to explain why California has to be the only state that pursues diesel fumes and small particulates with no regard for the strength of the health effects research and certainly no regard for the economic consequences for an economy dependent on diesel engines. There is no good reason at this time for another round of air pollution regulations focused on diesel and small particles.

ON A MORE PERSONAL AND DIRECT NOTE, I CHALLENGE DR. UTELL, WHO WAS ENGAGED AS A CARB EXPERT, WHO IS WELL KNOWN NATIONALLY TO BE A COMPETENT AND INSIGHTFUL RESEARCHER, TO SAY AND WRITE, ONE WAY OR THE OTHER, IF HE THINKS CURRENT LEVELS OF AMBIENT AIR POLLUTION, DIESEL FUMES, SMALL PARTICLES, OR ANY OTHER POLLUTANT, KILL ANYONE, ANYTIME, ANYWHERE IN AMERICA.

I know that Dr. Utell, like any good clinician/critical care specialist, could keep a patient with three alveoli and a bronchus alive indefinitely and that he knows that toxicology is not a desk and computer game. Epidemiology is out of control and producing junky studies of all kinds to the detriment of policy makers in California and nationally.

I can understand how fanatics with a career at stake, who have Ph.D.s in physics and public health and economics and such can pretend that people actually die on the desk in a death certificate, but my challenge is to the physicians of the epidemiology community—THE Jon Samets and Mark Utells of the epidemiology community. Tell this benighted emergency physician why we all should believe that non toxic ambient air pollution kills people and the CARB can make claims of thousands of innocent Californians will die prematurely because of diesel or dust in the air?

It appears that these studies are mischievous and deceptive and they will panic politicians to do more to hurt the California economy for no real benefit to the citizens of California.

People do not die of air pollution in America. The bad old days of London and Pittsburg dirty air are gone. Modern medicine would have saved those folks too because the last 50 years have completely changed our ability to treat respiratory illness. Air quality in California, the rest of America is benign and getting better all the time. CARB refuses to tell the truth on that, instead focusing on the negative.

The days of the killer smog and soot in America are gone. This panic mongering has to stop and physicians in public health research have a professional duty to shut up the chicken littles. Regulatory and economic burdens of new CARB regimes of air quality controls, chasing after small particles and diesel exhaust, will jeopardize the economic well being of the state of California and its residents. It is well known in public health epidemiology that poverty is an independent predictor of premature deaths. Will CARB be responsible for those deaths created by lost jobs and other economic hardships? Those will be real deaths, not the desk top toxin deaths predicted by the CARB.

Respectfully submitted,

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James Enstrom, UCLA, Los Angeles, CA

Comments Regarding May 22, 2008 CARB Draft Staff Report "Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California"

(http://www.arb.ca.gov/research/health/pm-mort/pm-mortdraft.pdf)

James E. Enstrom, Ph.D., M.P.H.
University of California, Los Angeles

July 11, 2008

1) Mischaracterization of 2005 Enstrom Paper

The CARB Draft Staff Report seriously mischaracterizes my 2005 paper (Inhalation Toxicology 17:803-816, 2005 http://www.scientificintegrityinstitute.org/IT121505.pdf). Numerous statements on page 22 are inaccurate. The methodology used in my study is completely consistent with the methodology used in the 2002 Pope study. For instance, my study controlled for smoking at entry and presented results for never smokers. Furthermore, fully adjusted relative risks hardly differed from age-adjusted relative risks. My study used the same 1979-1983 PM2.5 data that was used in the Pope studies and these underlying US EPA data were presented in a clear and well-defined manner. Although it is the largest and most detailed study ever published on PM2.5 and mortality in a California population, my study was not used by CARB staff to calculate the relationship between PM2.5 and mortality in California. CARB staff should fairly and accurately describe and use my study.

2) Omission of 2006 Enstrom Response to 2006 Brunekreef Criticism

Although the CARB Draft Staff Report cited the 2006 Brunekreef criticism of my 2005 paper, the Report completely omitted my 2006 response to Brunekreef (Inhalation Toxicology 18:509514, 2006 http://www.scientificintegrityinstitute.org/IT060106.pdf). My 2006 response addressed in a detailed manner the criticism of my 2005 paper and needs to be fully considered and cited by the CARB staff in their comments about my study.

3) Failure to Respond to April 22, 2008 Enstrom Public Comments to CARB

CARB Staff and the CARB Draft Staff Report have failed to address the important points made in four pages of public comments submitted to CARB on April 22, 2008 regarding the Goods Movement Emission Reduction Plan and the health effects of diesel emissions (http://www.arb.ca.gov/lists/erplan08/2-carb_enstrom_comments_on_gmerp_042208.pdf). In particular, the CARB Draft Staff Report fails to mention the California specific epidemiologic evidence in the 2000 HEI Reanalysis Report by Krewski et al. (http://pubs.healtheffects.org/view.php?id=6, Part II, page 197). The US map of "fine particles and mortality risk" on page 197 indicates no excess mortality risk in California due to PM2.5 among the ACS CPS II cohort during 1982-1989. This finding that is consistent with the results in my 2005 study, which is based on the California portion of ACS CPS I (CA CPS I). All of the points in my public comments should be addressed, because they are relevant to CARB Draft Staff Report.

4) Proposed Calculation of California-specific Relative Risks in ACS CPS II Cohort
Using same ACS CPS II database and proportional hazards methodology used in Pope et al. study (JAMA 2002;287:1132-1141 http://jama.ama-assn.org/cgi/reprint/287/9/1132), calculate all cause mortality relative risk (RR) and 95% confidence interval (CI) associated with a 10µg/m^3 increase in PM2.5, similar to RRs shown in JAMA Table 2.

a) Calculate age-sex-adjusted RRs and fully adjusted RRs based on all 61 metropolitan areas for 1979-1983, 1999-2000, and average PM2.5 related to all causes of death during three time periods: September 1, 1982 through December 31, 1998, September 1, 1982 through December 31, 1989, and January 1, 1990 through December 31, 1998 [2 x 3 x 3 = 18 RRs]. For instance, fully adjusted RR (1979-1983 PM2.5 , 1982-1998 deaths) = 1.04 (1.01-1.08).

b) Calculate age-sex-adjusted RRs and fully adjusted RRs based on the metropolitan areas in California for 1979-1983, 1999-2000, and average PM2.5 related to all causes of death for the three time periods: 1982-1998, 1982-1989, and 1990-1998 [2 x 3 x 3 = 18 RRs]. Specify the definition of the California metropolitan areas used in the JAMA paper and the number of CPS II subjects and deaths in each area used in the calculation of each RR.

c) Calculate age-sex-adjusted RRs and fully adjusted RRs based on the eleven California counties shown in Table A for 1979-1983, 1999-2001, and average PM2.5 related to all causes of death for the three time periods: 1982-1998, 1982-1989, and 1990-1998 [2 x 3 x 3 = 18 RRs]. Specify the number of CPS II subjects and deaths in each county used in the calculation of each RR.

PM2.5 (µg/m^3)

Table A. Fine particulate matter levels, PM2.5 (µg/m^3), in 11 California counties from the 1979-1983 Inhalable Particulate Network (IPN) and 1999-2001 Aerometric Information Retrieval System (AIRS) of the EPA (Enstrom *Inhalation Toxicology* 17:803-816, 2005 http://www.scientificintegrityinstitute.org/IT121505.pdf and Enstrom *Inhalation Toxicology* 18:509-514, 2006 http://www.scientificintegrityinstitute.org/IT060106.pdf).

California county	1979-1983	1999-2001	Average 1979-1983/1999-2001
Santa Barbara	10.6	10.7	10.65
Contra Costa	13.9	14.0	13.95
Alameda	14.4	14.4	14.4
Butte	15.5	15.4	15.45
San Francisco	16.4	15.4	15.9
Santa Clara	17.8	17.0	17.4
Fresno	18.4	20.2	19.3
San Diego	18.9	15.2	17.05
Los Angeles	28.2	20.4	24.3
Kern	30.9	19.4	25.15
Riverside	42.0	21.1	31.55

5) July 11, 2008 Teleconference Involving Epidemiologists and CARB Staff

A July 11, 2008 teleconference was organized by Hien Tran, Ph.D., in response to concerns that I have raised in the above four points and in other forums during the past few months. This teleconference included me and several other epidemiologists and CARB staff involved with producing the May 22, 2008 Draft Staff Report. As a result of this teleconference, I have the following tentative conclusions:

a) The CARB staff indicated a willingness to revise the Draft Staff Report in order to accurately characterize my 2005 study and my 2006 response to the 2006 Brunekreef criticism. However, given the relatively low evaluation that my paper was given in Tables 2a and 2b by the twelve experts involved in the elicitation process, it is unlikely that CARB staff will actually use the California specific results in my paper in developing the final relationship between PM2.5 and premature deaths in California.

b) The twelve experts involved in the elicitation process do not represent the full range of opinions on the epidemiologic relationship between PM2.5 and mortality in California. Particularly troubling is the fact that many of the experts evaluated their own research. Five of the experts were co-authors on the four highest rated studies in Table 2a and on the five highest rated studies in Table 2b. Because of the heavy reliance on the opinions of these twelve experts, the Draft Staff Report does not present a fair and balanced assessment of all relevant California specific evidence.

c) Other than myself, the teleconference epidemiologists expressed great reluctance toward conducting the CPS II analyses that I proposed in point 4). These analyses would produce new California specific evidence based on the CPS II cohort. This evidence would add substantially to the California specific evidence in my 2005 paper. It is very important that these analyses be undertaken and I intend to make an effort to see that they are conducted.

d) Particularly troubling is the fact that CARB is currently funding extensive new analyses of PM2.5 and mortality in the CPS II cohort, but not the analyses that I proposed in point 4). The analyses in point 4) involve determining the California specific results within the nationwide Pope 2002 study, which is the highest rated study in Tables 2a and 2b. Because of the economic consequences associated with the CARB assessment of the relationship between PM2.5 and mortality in California, it is very important that CARB fund all relevant assessments of this relationship.

e) As I made clear, I am willing to work with CARB staff and the teleconference epidemiologists in conducting additional relevant analyses of my CA CPS I cohort and the ACS CPS II cohort. In the interest of determining the most accurate and reliable relationship between PM2.5 and mortality in California, hopefully the CARB staff and teleconference epidemiologists will work with me and other epidemiologists who can provide relevant expertise on this subject.

Union of Concerned Scientist and Environmental Defense Fund

July 11, 2008

Dr. Hien Tran
California Air Resources Board
Research Division 1001 I Street
P.O. Box 2815 Sacramento, CA 95812

Re: Methodology Update to Estimate Premature Death Associated with Fine Airborne Particulate Matter Exposures

Dear Dr. Tran,

The Union of Concerned Scientists and Environmental Defense Fund applaud the Air Resources Board (ARB) for your continued commitment to further our understanding of the health impacts of air pollution in California. The ARB's leadership in air pollution science, health effects research, and air quality regulation is critical to protecting both California's public and economic health. The proposed update to the methodology for estimating premature deaths from exposure to fine particulates furthers our understanding of the human health impact of air pollution and the potential benefits of taking action to clean the state's air.

We support ARB's use of a robust scientific peer and public review process in developing the May 22nd draft *Methodology for Estimating Premature Deaths Associated with Long-term Exposures to Fine Airborne Particulate Matter in California*. Over the past four years, numerous new analyses, as well as follow-up studies of previous cohorts, have expanded the literature on the health effects of PM2.5 exposure. Incorporation of these recent study results into ARB's methodology for estimating premature deaths, as well as consideration of US EPA's solicitation of experts, adds to the robustness of estimates of premature death in California and elevates the importance of reducing exposure to PM2.5.

ARB has suggested approaches to determining a PM2.5 concentration threshold for the calculation of reduction of premature mortality benefits for regulatory impact analysis.. Given the uncertainty and lack of empirical data supporting a threshold, we believe ARB's proposal to include a range of estimates from background levels to the lowest level of PM2.5 measured in the American Cancer Society cohort study an appropriate interim solution. As additional data and research is performed on threshold limits of health effects, ARB should reevaluate its methodologies and assumptions and update them as appropriate.

As California moves forward in its struggle to protect its residents from air pollution throughout the state, ARB must continue to understand the latest air pollution science and health effects research. In order to provide all California clean and healthy air, ARB should continue to update and revise health calculations based on the latest available

peer-reviewed publications and studies, improve upon our understanding of emission sources to better target emission reduction efforts, and support health effects

We commend ARB staff for undertaking the significant effort of updating the methodology through a peer reviewed and open public process in order to support the development of effective emissions control measures and thank you for the opportunity for comment.

Sincerely,

Don Anair Senior Analyst
Union of Concerned Scientists

Camille Kustin Policy Analyst
Environmental Defense Fund