**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**
**WASHINGTON D.C. 20460**

December 17, 2003

OFFICE OF
THE ADMINISTRATOR
EPA SCIENCE ADVISORY BOARD

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The attached draft report of the Health Effects Subcommittee (HES) of the Advisory Council on Clean Air Compliance Analysis (COUNCIL) is still undergoing discussion and review. Once discussed by the HES and the COUNCIL at public sessions, and after approval by the COUNCIL, it will be transmitted to the EPA Administrator and become available to the interested public as a final report.

This draft has been released for general information to members of the interested public and to EPA staff. The reader should remember that this is an unapproved working draft and that the document should not be used to represent official EPA or Council views or advice. Draft documents at this stage of the process often undergo significant revisions before the final version is approved and published.

The SAB Staff Office is not soliciting comments on the advice contained herein. However, as a courtesy to the EPA Program Office that is the subject of the review, we have asked the Program Office to respond to the issues listed below. Consistent with SAB policy on this matter, the Council is not obligated to address any responses it receives.

1. Has the Subcommittee adequately responded to the questions posed in the Charge?
2. Are any statements or responses made in the draft unclear?
3. Are there any technical errors?

For further information or to respond to the questions above, please contact:

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# Advisory on Plans for Health Effects Analysis Presented in the May 12, 2003 Analytical Plan for EPA's Second Prospective Analysis – Benefits and Costs of the Clean Air Act, 1990-2020: An Advisory by the Health Effects Subcommittee of the Advisory Council for Clean Air Compliance Analysis

Insert Date

EPA-SAB-COUNCIL-ADV-03-00x

Governor Michael O. Leavitt
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Advisory on Plans for Health Effects Analysis in the Analytical Plan for EPA's Second Prospective Analysis – Benefits and Costs of the Clean Air Act, 1990-2020: An Advisory by the Health Effects Subcommittee of the Advisory Council for Clean Air Compliance Analysis

Dear Governor Leavitt:

The Advisory Council on Clean Air Compliance Analysis met on (insert date) to discuss this Advisory provided by its Health Effects Subcommittee on the Agency's plans for health effects analyses in the upcoming Second Prospective Analysis of the costs and benefits of the Clean Air Act. The Health Effects Subcommittee (HES) met in a public session, August 27-29, 2003 to consider in detail charge questions from the Agency related to a wide range of health effects to be addressed in the Second Prospective Analysis.

The Council and the HES are guided in this Advisory by the Agency's charge from Congress in Section 812 of the Clean Air Act Amendments of 1990 that the mandated analyses be "comprehensive" and "that the Administrator shall consider all of the economic, public health, and environmental benefits of efforts to comply. In any case where numerical values are assigned to such benefits, a default assumption of zero value shall not be assigned to such benefits unless supported by specific data."

The Council and the HES provide this advice to assist the Agency in fully characterizing the science related to health effects related to the Clean Air Act. We point out that now, as in the past, major categories of effects will be left unquantified such as cardiovascular morbidity from long-term exposure, ecological effects and most air toxics health effects, because of the limitations of existing scientific methods and data. The HES appreciates the efforts made by EPA's Project Team to expand benefit categories to be captured in the Second Prospective Analysis in their exhaustive review of a wealth of new scientific literature and their efforts to capture the uncertainties associated with that new literature.

The HES and the Council generally support EPA's Analytic Plan. There are two issues, however, which we believe deserve more careful attention. One is the Agency's exploration of the use of formal expert judgment as a means for characterizing uncertainty. The second is the omission of infant mortality effects and exacerbation of asthma from the base case analysis in the study.

We applaud the Agency's interest in exploring the use of formal expert judgment as a tool for improving uncertainty analysis and believe that the proposed pilot study has great potential to yield important insights. The pilot is well-designed to inform subsequent and more comprehensive expert elicitation projects, but relies on the opinions of a relatively small group of experts. It may provide preliminary information about the general magnitude of the mortality effects, and may yield a sense of both the uncertainty inherent in these estimates and the factors largely responsible for such uncertainty. However, until the pilot study methods and results have been subjected to peer review, it may be unwise for the Agency to rely directly on these preliminary results in key policy decisions.

On the second matter, i.e. the omission of infant mortality and asthma exacerbation, we strongly recommend that the Agency redesign the analysis to include these effects in their base case.

In regard to the base case for the study, we strongly advise that the Agency should continue to use prospective cohort studies as the basis for analysis of mortality. We propose that the Second Prospective Analysis present the base case with associated uncertainties (preferably with summary 10%-90% confidence boundss), plus a set of sensitivity analyses, rather than the base case and a single "alternative analysis." The Council and the HES advise that the single "alternative analysis" to the base case described in the Agency's Draft Analytical Plan does not represent to us, as scientific and technical experts, the comprehensive scientific analysis of health benefits that we understand the Clean Air Act to require. We advise that the Agency aim for quantitative base case estimates that prudently include all health effects for which there is reasonable quantitative evidence with careful avoidance of potential double counting and then acknowledge expected benefits that cannot be adequately quantified at this time. If alternative estimates are presented, they should be balanced to reflect the possibilities that the base case may either understate or overstate actual health benefits. We also support EPA's plans for meta-analyses for ozone mortality and the Agency's plans to consider adding it to base case analysis, subsequent to review of the results of those analyses.

We appreciate the opportunity to review the Analytical Plan and to provide you with advice on the analysis of health effects. The HES would be pleased to expand on any of the findings described in this report and we look forward to your response

.

Sincerely,

Dr. Bart Ostro, Chair
Health Effects Subcommittee

Dr. Trudy Ann Cameron, Chair
Advisory Council on Clean Air
Compliance Analysis

# NOTICE

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**U.S. Environmental Protection Agency**

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# 1. EXECUTIVE SUMMARY

In this Advisory, the Health Effects Subcommittee (HES) of the Advisory Council on Clean Air Compliance Analysis provides detailed advice related to a wide range of health effects to be addressed in the Second Prospective Analysis. The overall purpose of the Advisory is to assist the Agency in fully characterizing the science associated with health effects related to the Clean Air Act.

The HES generally supports EPA's Analytic Plan. There are two major issues, however, which it singled out for more careful attention. One is the Agency's exploration of the use of formal expert judgment as a means for characterizing uncertainty. The second is the omission of two important effects, infant mortality and exacerbation of asthma from the base case analysis in the study.

The HES supports the Agency's interest in exploring the use of formal expert judgment as a tool for improving uncertainty analysis and believes that the proposed pilot study has great potential to yield important insights. It notes, however that although the pilot is well-designed to inform subsequent and more comprehensive expert elicitation projects, it relies on the opinions of a relatively small group of experts. It may provide preliminary information about the general magnitude of the mortality effects, and may yield a sense of both the uncertainty inherent in these estimates and the factors largely responsible for such uncertainty. However, until the pilot study methods and results have been subjected to peer-review, it may be unwise for the Agency to rely directly on these preliminary results in key policy decisions.

In regard to the omission of infant mortality and asthma exacerbation, the HES advises that the Agency redesign the analysis to include these effects in the base case.

In regard to the base case for the study, the HES recommends that the Agency continue to use prospective cohort studies as the basis for analysis of mortality. The HES advises that the Second Prospective Analysis present the base case with associated uncertainties (preferably confidence intervals of 90% and 10%), plus a set of sensitivity analyses, rather than the base case and a single "alternative analysis."

In addition to these major points, the HES provides advice on many detailed charge questions. This summary identifies that advice briefly. The HES advises the Agency on the use of alternative data or methods for characterizing: ozone effects: covariation with particulate matter (PM); source-specific concentration-response (C-R) functions; extrapolation to other age groups; exposure assessment (use of grids); infant effects; asthma effects; and the effects of sulfur dioxide ($SO_2$), nitrogen dioxide ($NO_2$), carbon monoxide (CO) (the SONOCO Suite).

The HES generally indicates support for the Agency's incorporation of several new and revised endpoints for PM, and suggests some modifications to the Agency's approach. The HES commends the EPA for its efforts to identify appropriate databases to update and strengthen population characteristics and health outcome rates. It identified, however, some remaining issues

concerning data sources and the uses of the data that need to be considered in further detail before the plan is implemented.

In regard to several questions related to the scientific merits of alternative methods for estimating the incidences of PM-related premature mortality, the Subcommittee agrees with EPA's current proposal to use prospective cohort-based estimates in the base case. Different cohort studies and, within each study, various C-R functions are available, using different causes of death, exposure windows, subgroups, and models. The HES recommends that the base case rely on the Pope et al. (2002) study and that EPA use total mortality estimates, rather than separate cause-specific estimates.

The HES advises the Agency on available data regarding mortality effects of non-fatal cardiovascular and respiratory events. It also provides advice on how to address the question of cessation lag. Regarding this last point, the HES notes that for long-term effects, empirical evidence is lacking to inform the choice of the lag distribution directly. Given that problem, the HES recommends that the Agency derive models for each cause of death category considered in the Second Prospective Study, since the lag structure most likely differs for different health problems.

The Subcommittee endorses EPA’s plans to sponsor three new meta-analyses of ozone mortality impacts to help characterize the independent health effects of ozone. It provides advice concerning how to address issues raised regarding aggregation and presentation of analytical results from the planned health analysis.

The HES concludes that the Agency’s proposed revised approach to determining costs and benefits of controls to limit stratospheric ozone reductions by anthropogenic chemicals is sound and addresses the issue comprehensively. The HES also notes that the Agency’s basic conception of the air toxics case study is reasonable, given that the chemical chosen, benzene, is data rich. Several suggestions for strengthening the approach are also provided. Finally, the HES makes several recommendations for the Agency to consider regarding the proposal to use a five-year cessation lag for benzene-induced leukemia.

# 2. INTRODUCTION

## 2.1. Background on this Advisory

The purpose of this Advisory is to provide commentary and guidance on EPA plans for developing the health effects analysis emissions inventories described in the July 8, 2003 review document, *Benefits and Costs of the Clean Air Act 1990-2020: Revised Analytical Plan for EPA's Second Prospective Analysis* (Analytical Plan).

The Health Effects Subcommittee (HES) of the Advisory Council on Clean Air Compliance Analysis (Council) held a public meeting on August 27-29, 2003 to receive briefings and discuss the charge questions provided by the Agency related to health effects analysis for the Analytical Plan. In addition to the Chair of the HES, who represents the HES on the Council, one additional member of the Council, Ms. Lauraine Chestnut, participated in this meeting. Four other members of the Council's Special Council Panel for the Review of the Third 812 Analysis,[1] who were added to the Council especially to address issues associated with analysis of uncertainty and statistical and subjective probability, joined the meeting either in person, by teleconference or by providing written comments for consideration during the Subcommittee meeting. In their discussions, members focused on issues related to the Agency's plan to develop health effects estimates. The charge questions are discussed in Section 2.2. and listed in Appendix A.

During the meeting in August, the Chair of the HES, Dr. Bart Ostro, provided information that he was considering serving as one of the five experts to be elicited by the Agency for a pilot study of premature mortality from exposure to particulate matter. That pilot is the subject of Charge Question 29. After the meeting, Dr. Ostro indeed decided to serve as one of the experts and also agreed to recuse himself from HES and Council deliberations on this question. Dr. Nino Kuenzli from the HES was appointed by the SAB Staff Office as the HES chair for discussions of this question.

The HES held an additional public teleconference on October 30, 2003 and then the Council held a public teleconference meeting on (insert date when discussions will happen) to discuss and formalize the advice to the EPA Administrator on this topic.

[1] Dr. John Evans, Senior Lecturer on Environmental Science, Harvard University; Dr. Dale Hattis, Research Professor, Center for Technology, Environment, and Development, George Perkins Marsh Institute, Clark University; Dr. D. Warner North, President, NorthWorks Inc; Dr. Thomas S. Wallsten, Professor, Department of Psychology , University of Maryland;

## 2.2 Charge Questions Related to Health Effects

In its review of the analytical plan, the Council and its subcommittees are guided by the Council mandate, as identified in the Clean Air Act (CAA) Amendments of 1990,[2]

a) Are the input data used for each component of the analysis sufficiently valid and reliable for the intended analytical purpose?

b) Are the models, and the methodologies they employ, used for each component of the analysis sufficiently valid and reliable for the intended analytical purpose?

c) If the answer to either of the two questions above is negative, what specific alternative assumptions, data or methodologies does the Council recommend the Agency consider using for the second prospective analysis?

In addition to this mandate, the Council received thirty-seven charge questions related to the draft analytical plan. Among those thirty-seven charge questions provided to the Council, fourteen charge questions related to health effects, uncertainty analysis of health effects, plans related to data quality and intermediate data products, results aggregation and reporting, uncertainty, stratospheric ozone analysis, and an air toxics case study. These Charge Questions are excerpted from the list of charge questions provided by the Agency on July 8, 2003 and listed in Appendix A to this Report. The charge questions listed there and addressed in this report by the HES retain the numbering scheme provided by the Agency in July.

[2]Specifically, subsection (g) of CAA 312 (as amended by Section 812 of the amendments) states: "*(g) The Council shall -- (1) review the data to be used for any analysis required under this section and make recommendations to the Administrator on the use of such data, (2) review the methodology used to analyze such data and make recommendations to the Administrator on the use of such methodology; and (3) prior to issuance of a report required under subsection (d) or (e), review the findings of such report, and make recommendations to the Administrator concerning the validity and utility of such findings.*"

# 3. RESPONSES TO CHARGE QUESTIONS

Agency Charge Question 11. Plans for estimating, evaluating, and reporting changes in health effect outcomes between scenarios

Charge Question 11. Does the Council support the plans described in chapter 6 for estimating, evaluating, and reporting changes in health effect outcomes between scenarios? If there are particular elements of these plans which the Council does not support, are there alternative data or methods the Council recommends?

HES Response: The HES provides here comments not specifically addressed in other formal charge questions posed by the Agency.

a. Ozone effects and issue of covariation with Particulate Matter (PM).

The underlying consideration here is whether ozone effects can be added to those based on C-R functions for PM without double counting. In the case of short-term exposure endpoints, the risks of doing so to any substantial extent are small because PM and ozone concentrations tend to be the least correlated of the criteria pollutants. For some endpoints, it will be possible to estimate risk ratios from two-pollutant (ozone and PM) models, where the estimate for each is adjusted for the other. This is one technique, albeit with some remaining possibility for misattribution, to minimize the possibility of double counting. However, since the co-variation of PM and ozone is often low, this is not a requirement. Several studies now suggest that daily exposure to ozone is associated with both daily mortality and morbidity, such as hospital admissions. Some of these findings have been demonstrated in season-specific analysis (Samet et al., 2000), which could then be used in the Section 812 Analysis. The HES urges caution, however, in basing estimates on C-R functions derived solely from studies conducted in the northeastern U.S. and southeastern Canada, where ozone and sulfates tend to be highly correlated. To the extent that pollution-specific evidence is drawn from data where the correlations between the pollutants are low, HES suggests that ozone-specific estimates be included in the aggregate estimates.

In the case of long-term exposures and mortality, EPA has correctly decided not to attribute any mortality effects to long-term exposure to ozone given the lack of any evidence supporting an independent effect. The ACS follow-up study (Pope et al., 2002) found no association between mortality and long-term average ambient ozone concentration.

b. Source-Specific Concentration-Response (C-R) Functions.

Regarding the term C-R functions, the Subcommittee notes that Chapter 6 (e.g. pages 6-1 and 6-2) uses the term C-R functions interchangeably for: 1) the concentration-response function epidemiologic studies used to quantify the association and 2) the "impact function" or "attributable case function." This latter function not only uses the epidemiology-based C-R function, but also the pollution level, the population size, and the baseline frequency of the outcome as input. The Subcommittee advises ***not*** to use one term for both, as this creates

confusion in discussions of various aspects, including uncertainties (e.g., 'impact function' faces more uncertainties than the C-R function).

There are only a few source-specific C-R functions currently available for species of PM and the Agency does not propose to use them in the Section 812 Analysis. For example, Laden et al. (2000), using source apportionment in the Boston area concluded that traffic-related pollutants and coal combustion-related particles were significantly related to short-term mortality, while soil-derived particles were not, with traffic-related particles having the largest effect. Hoek et al. (2000) concluded that annual mortality was significantly related to proximity to heavily traveled roadways, particularly for those with high volumes of truck traffic. However, for the application of these studies to the 812 Analysis, one would also need the exposure distribution data for these source-specific surrogates, for the U.S., which are not readily available. Thus, it still is appropriate to make calculations based on PM2.5, rather than source-specific PM. It is important, however, to describe what the most important sources are for PM. Specifically, it would be of interest to provide estimates of the contributions of various sources to the ambient PM, including both primary and secondary processes. The health impact of a specific source may be larger or smaller than its relative contribution to the ambient PM concentration, as toxicities may be source dependent. This should also be discussed in the Agency's analysis.

The issue of a special role for traffic-related air pollution is complicated by the strong spatial gradient of primary pollutants from traffic sources. Studies around California freeways indicated that ultrafine particle numbers can vary by an order of magnitude within100 meters, carbon monoxide and nitrogen oxides by somewhat smaller ratios, while PM2.5 mass, which is dominated by regional background, shows little variation with proximity to traffic (Zhu et al., 2002). Furthermore, the regional ozone is greatly reduced near the freeway due to its scavenging by nitric oxide. These spatial variations are important for some health effects. Recent animal inhalation studies conducted at varying distances from a freeway show effects for close-in animals not seen for animals exposed at greater distances (Lippmann et al., 2003). These studies complement the observations of human populations in relation to roadway proximity (Hoek et al., 2002, Laden et al., 2000, Venn et al., 2001)

The cost-benefit analyses for 812 cannot quantitatively address this issue of traffic-related pollution effects because its grid-based exposure estimates are based on much larger spatial elements. The available database remains inadequate for the disaggregation of concentration-response relationships by pollutant source category. However, the HES recommends that the Second Prospective 812 Analysis consider conducting some sensitivity analysis that incorporates the limited information on relative toxicities.

c. Extrapolation to Other Age Groups.

For mortality associated with long-term pollution exposure, extrapolation of the C-R relations to adult age-groups younger than those studied in the epidemiologic reports would be unnecessary. For chronic disease related endpoints, the baseline frequency increases rapidly with age and the public health impact for adult ages below about 30 can be expected to be too small to significantly affect the totals obtained from the listed C-R functions. An exception to this would be made if the Harvard six-city cohort were used in a sensitivity analysis, since this cohort

included participants who were age 25 and above.

For health effects other than mortality, EPA should strongly consider broadening the age ranges beyond those included in the original studies that established the risk coefficients. In general, the age ranges studied were limited more by population access or study design considerations than by real restrictions on effects to the age group studied. Therefore, the age range should be expanded where there is some reasonable physiological basis for expecting that the effects occur among a wider range of ages (e.g., applying C-R functions to all children rather than just the ages of school children in the original study).

d. Exposure Assessment (Use of Grids).

The exposure assessment approach utilizes the best available data and models. However, uncertainties remain large in this area – and the magnitude of these uncertainties will require better characterization in the second prospective analysis. Additional uncertainties arise in the translation of modeling results to population-relevant concentration estimates. In the case of ozone, the procedure involves modeling three multi-day episodes for the eastern US and two multi-day episodes in the western US. Each episode is approximately of one-two week's duration. These brief modeling results are then extrapolated to the entire ozone season by reference to observed data available from AIRS. The result is a grid of 12x12 km hourly (ozone) or daily (PM) concentrations estimates that cover the continental US. EPA should work towards extending the modeling so that it covers longer, more representative periods, with less reliance on temporal extrapolation. In addition, there is a need to estimate uncertainties associated with this extrapolation.

Block-level data from the 2000 U.S. Census are used to develop population estimates corresponding to the grid resolution of each air quality model (e.g. 12x12 km for ozone and 36x36 km for PM).gg Health impacts are then estimated by applying epidemiologically derived C-R functions to the concentration, population, and baseline outcome rates for each grid. There is some question about the impacts of using these grid average concentration estimates as inputs to C-R functions which were derived from epidemiology studies in which a different sort of exposure measure is used (i.e., the concentrations at one or several population-oriented monitors) across a metropolitan area. There may not be a problem since both the pre- and post-control scenarios use the same (potentially biased) configuration. However, this should be discussed and verified. Center-city monitors may over-estimate some population exposures in epidemiology studies whereas the gridded concentrations provide a broader, area-wide exposure estimate. The Subcommittee suggests that EPA do a sensitivity analysis in which the health assessment is repeated using the mean of the estimated concentrations for the grids in which monitors are located in a selected urban area, for example. This could be compared to the standard assessment results to see how big the differences are.

The Subcommittee also wishes to emphasize the need for efforts to improve exposure modeling and health assessment for people living near roadways and other local sources. A growing literature has emphasized the importance of roadway proximity as a risk factor for both elevated exposures and adverse health outcomes (Zhu et al., 2002; Brunekreef et al., 1997; Hoek et al., 2000).

e. Infant effects.

The Subcommittee proposes that EPA include effects of air pollution on infant mortality rates in the base estimates. In recent years, several international studies addressed the association of ambient air pollution and death during the first year of life. The outcome has also been included in the 2002 World Health Organization Global Burden of Disease study on ambient air (Ezzati et al., 2002). The WHO report relied on several time-series studies that relate daily exposures to PM to mortality for children under age five. The findings of effects of ambient air pollutants on respiratory inflammation in children support the evidence of effects on infants where respiratory infections are a major cause of infant deaths. The evidence for air pollutants to promote respiratory infections in infants has recently been corroborated (Belanger et al., 2003). A further argument to include infant mortality is the availability of effect estimates from a large U.S. cohort study conducted by Woodruff et al. (1997). It is based on ~4 million infants born 1989-91 in 86 metropolitan areas. Exposure was defined as the mean outdoor PM10 levels for the first two months of life. Woodruff et al. controlled for some individual risk factors for infant mortality (i.e., maternal education, maternal ethnicity, parental marital status, maternal smoking during pregnancy) and other potential confounders (i.e., infants' month and year of birth, average temperature during first 2 months of life). They found that postneonatal mortality from all causes (excluding violent death) increased by 4% (95% confidence interval [CI] 2-7%) for every 10 $\mu g/m^3$ PM10. Sudden infant death syndrome (SIDS) and respiratory disease deaths in infants with normal birth weight increased by 12% (95% CI 7-17%) and 20% (95% CI 6-36%) for every 10$\mu g/m^3$ PM10, respectively.

The Subcommittee also notes a re-analysis of Lipfert (2000) that partly confirmed associations (for PM10 only). He used all U.S. infants born in 1990. However, exposure assignment was a larger non-systematic source of error in this study, as the annual 1990 mean was assigned to each infant, thus including pre- and post-mortem air quality data. The HES therefore recommends using the available studies (Woodruff et al., 1997, Chay and Greenstone, 2001) to derive quantitative estimates of infant mortality.

Unfortunately, it is difficult to estimate the lost years of life associated with these deaths. In the most extreme case, each air pollution-related infant death loses the total years of life (life expectancy at birth). In the other extreme, one may hypothesize that all these infants were susceptible for death at a young age no matter what levels of air pollution they would experience in the first weeks of life (harvesting only). In the latter case, air pollution would be considered of limited public health relevance for this outcome. So far, no infant mortality study has formally addressed the issue of harvesting. Therefore, the person time lost among infants is not known. This range of uncertainty needs to be addressed as part of the uncertainty analysis.

The Subcommittee also notes that the reference to Kaiser et al. 2001 in the Analytic Plan is misleading. Kaiser et al is not a study that investigates the association of air pollution with infant mortality. It is, however, a published abstract of an impact assessment that estimated the air pollution related burden of infant mortality. The assessment used the Woodruff et al. study as input information.

f. Asthma.

The Subcommittee proposes that EPA include asthma exacerbations for children and adults in the base case. The evidence for adverse effects of ambient air pollution, particularly PM and ozone, among asthmatics is sufficient to include it in the benefits analyses. On the other hand, the association of new onset of asthma (incidence of doctor's diagnosed asthma) is currently less clear and probably a more complex issue of interacting environmental and genetic factors. Thus, the Subcommittee suggests not including it in the base case assessment at this time. The Subcommittee advises the Agency not to use the term chronic asthma. Asthma is, by definition, a chronic obstructive disease with the level of obstruction being a function of exposure to various triggers, including air pollution. New onset of asthma; incidence of physician-diagnosed asthma; prevalence of doctor's diagnosed asthma etc. are more appropriate terms.

The Subcommittee acknowledges that dealing with asthma exacerbations is a challenge in the context of benefits assessment for the 812 Analysis. The definition of an asthma exacerbation varies across studies, and is partly determined by study design. Panel studies are able to monitor daily onset of symptoms or medication use, whereas cross-sectional or cohort studies usually ask about the occurrence or frequency of symptoms during the past year. Although all these approaches are useful avenues for epidemiological investigation, the methodological differences among studies make it difficult to apply their results for benefits assessments.

The difficulties are not primarily related to the choices of C-R functions but rather to the definition and the respective derivation of an appropriate background frequency of asthma attacks, and the assignment of a monetary value. The latter may depend on the severity of an exacerbation. Neither asthma nor exacerbations are consistently defined in the air pollution studies. Nevertheless, the Subcommittee recommends that the Agency include asthma exacerbation in the base case and rely on panel studies to derive a C-R function. In the selection of C-R function for asthma, the Subcommittee recommends selection of studies that have comparable design as well as similar baseline frequencies in both asthma prevalence and exacerbation rates. Among such a set of studies, C-R functions and background rates of exacerbations may be estimated (with distributions) for use in the 812 Analysis. The distribution of these parameters may be part of the uncertainty assessment. In the absence of population-based background frequency data, EPA may consider the use of frequency information provided in the studies used to derive the C-R function. Given the internal consistency of these studies, this choice may be more appropriate, thereby limiting uncertainties. The selection of studies used for the derivation of C-R functions and background frequencies may include more recent publications from western European studies, if those studies appear in the peer review literature. This may lead to a larger number of studies with comparable designs and, thus, more consistent results.

The determination of the age range for the quantification of asthma attacks or symptoms may be less restrictive than for other outcomes. The HES recommends in particular that the Agency consider extrapolating results to a wider age range than the original asthma studies in children. Studies in children usually restrict age ranges based on logistic rather than pathophysiologic reasons. The Committee considers it unlikely that exacerbations of symptoms

observed in children age 11 would not be observed among somewhat older or younger children. Thus, for the quantification of symptoms in children it is recommended to apply CR-functions to all children age 6 to 18. The exclusion of younger children is based on the uncertainty in the definition of asthma in early life, the exacerbation thereof, and the related CR-function for air pollution.

One may assume that, among asthmatics, a day with an exacerbation may be a day of restricted activity. Thus, the benefit derived for restricted-activity days may partly or fully include the asthma exacerbations. This has to be considered in the total assessment.

In the absence of independent response functions for PM and ozone, the Subcommittee recommends the Agency use only one pollutant as a surrogate for the whole effect, although this may underestimate the overall effect on asthmatics. This recommendation is in contrast to the recommendation the HES makes for mortality and hospital emissions, where effects from both particles and ozone should be estimated. This recommendation relating to asthma reflects the fact that there are many more single- and multipollutant studies available for mortality and hospital admissions than there are comparable studies on asthma attacks. This may, however, change in the future.

The 812 report should mention that the social costs of the effect of pollution on those with asthma are most likely underestimated since the epidemiological studies do not incorporate the treatment and averting behavior asthmatics may engage in to mitigate the adverse effects of air pollution.

g. Effects of Sulfur Dioxide ($SO_2$), Nitrogen Dioxide ($NO_2$), Carbon Monoxide (CO) (SONOCO Suite).

As outlined in Exhibit 6-1 in the Analytical Plan, a few selected endpoints for the SONOCO suite will be quantified and monetized, and a few have been selected for alternative or sensitivity analyses. The HES concurs with the use of the C-R functions as used in the FirstProspective Study as the best available estimates since little, if any, new work has been reported and with the plan to update these functions as new information becomes available during the 812 process. In supporting the quantification of some endpoints in relation to the SONOCO gases, the HES is not taking a view on causality or biological plausibility of these specific pollutants. Rather, the Subcommittee is assuming that, where they are used, C-R functions in these pollutants are quantifying adverse effects of some aspects of the pollution mixture which are not already taken into account via C-R functions in PM or ozone. Where C-R functions are used for each of the three gases, e.g. for respiratory hospital admissions, the HES asks that the possibility of double counting be considered and discussed, when aggregating across all pollutants quantified.

The HES advises that the Agency provide an expanded discussion of the following points on the Analysis. In regard to $SO_2$, the HES notes that Pope et al. (2002) show mortality associations for sulfur oxides, albeit there are also associations between SO2 and non-cardiopulmonary deaths as well. The HES advises that the Agency discuss the pros and cons of

possible inclusion of sulfur dioxide and mortality from longer-term exposure. In regard to nitrogen dioxide, European short-term effect studies suggest an interaction with PM (i.e., PM effects are increased in the presence of $NO_2$ and $NO_2$ is significantly associated with increased respiratory infections). It is not clear whether these will be included in the analysis. Interaction between pollutants is not discussed (i.e., ozone and $NO_2$ have more than additive effects in some toxicological studies). Finally, in regard to CO, the Subcommittee asks the Agency to consider and discuss whether non-asthma ER visits for respiratory or cardiovascular causes should be moved to the base case analysis.

Agency Charge Question 12: New and Revised Endpoints for Particulate Matter and Ozone

Charge Question 12. EPA seeks advice from the Council regarding the technical and scientific merits of incorporating several new or revised endpoint treatments in the current analysis. These health effect endpoints include:

a. Premature mortality from particulate matter in adults 30 and over, PM (Krewski et al., 2000);
b. A PM premature mortality supplemental calculation for adults 30 and over using the Pope 2002 ACS follow-up study with regional controls;
c. Hospital admissions for all cardiovascular causes in adults 20-64, PM (Moolgavkar et al., 2000);
d. ER visits for asthma in children 0-18, PM (Norris et al., 1999);
e. Non-fatal heart attacks, adults over 30, PM (Peters et al., 2001);
f. School loss days, Ozone (Gilliland et al., 2001; Chen et al., 2000);
g. Hospital admissions for all respiratory causes in children under 2, Ozone (Burnett et al., 2001); and,
h. Revised sources for concentration-response functions for hospital admission for pneumonia, COPD, and total cardiovascular: Samet et al., 2000 (a PM10 study), to Lippmann et al., 2000 and Moolgavkar, 2000 (PM2.5 studies).

HES Response: The HES comments regarding new endpoints used for particulate matter and ozone appear immediately below in separate sections

a. New and Revised Endpoints for Particulate Matter.

The HES generally supports the incorporation of the new and revised endpoints as indicated in charge questions 12. However, some modifications are suggested, specifically:

1. The Pope et al., 2002 should be used for the base estimate of premature mortality, rather than the Krewski et al., 2000. As indicated below, this data set adds nine years of data to the follow-up period, and additional exposure data. Some of the authors are the same as in the original study using the ACS and in the Krewski et al. 2000 study so they benefit from the insight gained by the Krewski reanalysis. In addition, the HES recommends using the risk estimates resulting from using all the years of exposure data, since this may serve to reduce measurement error. Sensitivity analysis for this endpoint could use other estimates from Pope et al. (2002), Krewski et al., 2000 and/or the results

of Dockery et al., 1993. Whichever is used, the choice should be explained in the Agency's assessment.

2. Estimates for hospital admissions studies (c and h) should utilize the large number of studies relating PM10 to both respiratory and cardiovascular admissions rather than simply rely on the Moolgavkar et al., 2000 and the Lippmann et al. 2000 of PM2.5. Estimates should be based on a meta-analysis of these studies conducted in multiple cites throughout the U.S. As such, they represent a broader range of conditions, co-pollutants, and climates than does reliance on any single study. In addition, the studies using PM10 incorporate the potential effects of coarse, as well as fine, particles. In the case of analysis related specifically to PM2.5, the use of the above studies is recommended if their impact is appreciably different from the results obtained by using the PM10-specific studies, adjusted for PM2.5.

3. As discussed above in Charge Question 11, several other endpoints should be added to the base case analysis including: (i) asthma exacerbations and PM10; and (ii) infant mortality and PM10 so that the base case will be more reflective of the comprehensive scientific analysis of health benefits that the Clean Air Act requires. In addition, as indicated above, the HES recommends that the age categories for the applied effects be increased when it is reasonable.

The Subcommittee also notes that EPA has five criteria to select C-R functions (page 6-10, top). The HES requests EPA to provide more explanation of how criterion 5 (biological plausibility) was applied

b. New and Revised Ozone Endpoints.

The Subcommittee concurs with EPA's two new endpoints related to ozone exposure. Gilliland et al. 2001 demonstrated acute associations between increased illness-related school absences among children enrolled in the California Children's Health Study (Hall et al., 2003). The study methods were thorough in terms of population characterization, exposure assessment and outcome assessment. Burnett et al., 2001, support respiratory hospital admissions for children under 2 years of age in relation to short-term ozone exposures.

Agency Charge Question 13 Baseline Data

Agency Charge Question 13: EPA seeks advice from the Council regarding the merits of applying updated data for baseline health effect incidences, prevalence rates, and other population characteristics as described in chapter 6. These updated incidence/prevalence data include:

a. Updated county-level mortality rates (all-cause, non-accidental, cardiopulmonary, lung cancer, COPD) from 1994-1996 to 1996-1998 using the CDC Wonder Database;
b. Updated hospitalization rates from 1994 to 1999 and switched from national rates to regional rates using 1999 National Hospital Discharge Survey results;
c. Developed regional emergency room visit rates using results of the 2000 National

Hospital Ambulatory Medical Care Survey;

d. Updated prevalence of asthma and chronic bronchitis to 1999 using results of the National Health Interview Survey (HIS), as reported by the American Lung Association (ALA), 2002;

e. Developed non-fatal heart attack incidence rates based on National Hospital Discharge Survey results;

f. Updated the national acute bronchitis incidence rate using HIS data as reported in ALA, 2002, Table 11;

g. Updated the work loss days rate using the 1996 HIS data, as reported in Adams, et al. 1999, Table 41;

h. Developed school absence rates using data from the National Center for Education Statistics and the 1996 HIS, as reported in Adams, et al., 1999, Table 46.

1. Developed baseline incidence rates for respiratory symptoms in asthmatics, based on epidemiological studies (Ostro et al. 2001; Vedal et al. 1998; Yu et al; 2000; McConnell et al., 1999; Pope et al., 1991).

HES Response: Overall, the Subcommittee commends the EPA for its efforts to identify appropriate databases to update and strengthen population characteristics and health outcome rates. There are some issues, however, that remain with the data sources and the use of the data that need to be considered in further detail before the plan is implemented. The HES highlights the major issues in comments here.

Fundamentally, baseline incidence rates are multipliers in the estimation of some health effects and therefore have a direct influence on the estimation of effects and potential benefits. In the first prospective analysis, preference was given to baseline incidence data at the county level, followed by national-level data. If those were not available, baseline incidence data for the study population were used to derive the impact functions. The primary data sources were the 1990 U.S. Vital Statistics and the 1997 National Hospital Discharge Survey (NHDS) of the Centers for Disease Control and Prevention. For the second prospective analysis, the baseline incidences will be adapted to match the specific populations studied and additional sources of information at the regional level are included for hospitalization rates and emergency room visits. These additions can be of some help in improving the accuracy of benefits calculations by location.

However, there are two factors that can alter the incidence rates as they are projected over time. One factor concerns differential incidence rates among multiple age groups. For example, the draft plan states that the baseline incidence rates for older populations are higher than the rates for younger populations. This statement relies on the assumption that the population age distribution will tend toward older ages over time. The demographic shift coupled with increased susceptibility for older individuals could lead to increased baseline incidence rates. The second factor concerns exogenous changes that may affect baseline incidence rates within a given age cohort. On page 6-15 of the Analytical Plan, paragraph 1, line 6 the Agency states, “baseline incidence rates…may decline slightly over time” without stating clearly which factors are involved in making this assumptions.

The HES notes that there are several factors to consider, in addition to age that can alter

incidence rates over time and recommends that EPA discuss these factors. For example, the demographic changes such as increasing proportions of minorities and economic factors may lead to decreasing health care access that may also increase baseline rates.

Although EPA states, "we will not attempt to estimate changes in baseline incidence rates," perhaps an analysis of rate trends retrospectively to 1990 or earlier could be useful in ascertaining how such changes contribute to overall uncertainty. EPA should evaluate whether there may be useful contrasts between the incidence rates used in the first analysis and the updated incidence rates that could shed some light on this issue.

While many of the data sources selected for the second prospective analysis are appropriate, some may need to be considered more thoroughly to appreciate their specific limitations before use in the cost-benefit analysis. The following themes emerged from the HES review of these data sources and exemplify the types of issues that need to be evaluated as EPA develops its analytic plans.

a. The number of persons or health events included in some of the national surveys may not be very large, particularly at the county level targeted in portions of draft. For example, EPA's plan to work with more than one year of the CDC Wonder data will help address this problem for many outcomes, but "missing" data will probably remain for several of the outcomes. This situation raises the question as to whether the use of particular health events may introduce a high level of uncertainty into the analysis. At the present time, the plan does not recognize this problem, discuss what level of "missing" data would be judged as unacceptable, or explain what alternative outcome categories or data sources would be used. The Subcommittee advises the Agency to distinguish between: (a) the spatial level on which the analysis is conducted, and (b) the spatial level at which results will be reported and conclusions will be drawn. It is likely that results for small areas will be (much) less reliable than for bigger ones, because often the small area input data will be average values from wider geographical regions, applied to all small areas of that region.

b. Selecting specific diagnostic codes within broad health outcome categories, as planned, is expected to provide health outcome estimates that more closely link to the results of epidemiological studies. However, if in these efforts to achieve a match, the outcome specification is too narrow (e.g., "acute bronchitis" instead of "all respiratory conditions"), small numbers will seriously reduce the reliability of the analysis. Therefore, careful consideration of the diagnostic codes to use with the related tradeoffs in uncertainty will be an important step in constructing the baseline datasets.

c. Additionally, there is concern that reliance on poorly defined diagnostic categories will result in estimates with a high degree of error. Examples of such categories or diagnoses include acute and chronic bronchitis, asthma exacerbation, school absence, etc. In these cases, the national dataset definitions should be compared to

the definitions used in epidemiological studies and a determination made as to whether the national sources will provide comparable outcome data. If the definitional differences are large, it may be more prudent to use the epidemiological studies to construct baseline rates, depending in part on the size of the baseline epidemiological studies and the representativeness of their populations.

d. The design of the national databases relies on complex sampling schemes that may or may not include sizable populations at risk for air pollution-related health effects. For example, the NHDS and the National Hospital Ambulatory Medical Care Survey (NHAMCS) use sampling designs that exclude specific types of hospitals and, as a result, exclude potentially sizable segments of the U.S. population (e.g., military and institutionalized persons). These groups may be at increased risk for important adverse outcomes of interest (e.g., heart attacks, chronic bronchitis, cancers, etc), which would then be undercounted by relying solely on the identified national data sets. Omitting these groups would bias the prevalence downwards and result in lower effect estimates. For outcomes where the exclusions may result in significant underestimates, careful consideration should be given to identifying additional data sources (e.g., databases for institutionalized persons, or the health care databases of the U.S. Department of Defense and/or Veterans Affairs) for otherwise excluded populations. Additionally, the HES recommends that EPA seek expert consultation from the National Center for Health Statistics (NCHS) for in depth information about the design of the selected databases and the limitations that need to be considered when applying the data for EPA's estimation purposes.[3]

e. The use of 1999 data from the National Health Interview Survey (NHIS) may present problems in the analysis. Despite the strength of having supplemental data on asthma outcomes, the 1999 survey relies on an unusually small sample size. This important limitation will probably result in "missing" data especially for county-level purposes. Whether the sample is so small that it will result in unreliable rates and thereby prevent the use of this year of data or whether its use only for specific analyses may be appropriate needs to be determined. If this year of data turns out to be unacceptable, the use of a more recent year with a larger sample size is recommended. The data may be sufficient for national or statewide conclusions, but not for small-area conclusions. The Subcommittee asks EPA to consider the extent to which the analysis will be (a) reported and (b) interpreted at small-area level.

f. The methods planned to construct the work loss and school absence rates are not clear in the documentation reviewed by the HES. For example, it is not clear which health condition(s) on the cited Tables 41 and 46 will be used or what level of relative standard errors will be judged as acceptable for estimation purposes. Additionally, which National Center for Education Statistics (U.S. Dept. of

[3] The Center's experts can be reached through www.cdc.gov/nchs/ or 301-458-4636.

Education) data will be used in combination with which NHIS data is not clear.

g. The epidemiological studies listed for developing the pediatric asthma symptom rates as a group provide good evidence. However, these studies depend on self-reported outcome data with little or no assessment of the reliability of the data; EPA should explore this issue with the authors. EPA staff is encouraged to contact the authors to obtain their judgments and any evidence or analyses on the reliability of the self-reported outcome data in their studies. Authors sometimes collect data for variables known to relate well to variables that are more subjective. When there are stable relationships between such variables, their correlation can be used to assess the reliability of the more subjective data. It would be useful to determine whether the authors have data that were or could be used to assess reliability; if not, then their best judgments of the self-reported data's reliability should be obtained.

The HES also noted that all of these papers studied populations living in the western United States. This observation raised the question as to whether the air pollution mix and/or the characteristics of the populations studied need to be evaluated to determine how relevant the results are for the entire U.S. population. If application of these epidemiological data to the U.S. population would introduce important uncertainties, then appropriate adjustments to reduce those uncertainties need to be identified. Application of these epidemiological data to the entire country may introduce additional uncertainty.

Agency Charge Question 14. Scientific merits of alternative methods to expert elicitation for estimating the incidences of PM-related premature mortality

Charge Question 14. EPA plans to initiate an expert elicitation process to develop a probability-based method for estimating changes in incidence of PM-related premature mortality. Plans for this expert elicitation are described in chapter 9 of this blueprint, and a separate charge question below requests advice from the Council pertaining to the merits of the design of this expert elicitation. EPA recognizes, however, the possibility that this expert elicitation process may not be fully successful and/or may not be completed in time to support the current 812 analysis. Therefore, in order to facilitate effective planning and execution of the early analytical steps which provide inputs to the concentration-response calculations, EPA seeks advice from the Council regarding the scientific merits of alternative methods for estimating the incidences of PM-related premature mortality, including advice pertaining to the most scientifically defensible choices for the following specific factors:

a. Use of cohort mortality studies, daily mortality studies, or some combination of the two types of studies
b. Selection of specific studies for estimating long-term and/or short-term mortality effects
c. Methods for addressing –either quantitatively or qualitatively– uncertain factors associated with the relevant concentration-response function(s), including
d. Shape of the PM mortality C-R function (e.g., existence of a threshold),
    1. PM causality,

2. PM component relative toxicity, and
3. PM mortality effect cessation lag structure
4. Cause of death and underlying health conditions for individuals dying prematurely due to chronic and/or short term exposures to particulate matter
5. The use of ambient measures of exposure for estimating chronic health effects, given recent research reviewed in the NAS (2002) report that questions the implications of using ambient measures in cohort studies

HES Response: The Subcommittee notes that there is some overlap between this Charge Question and Charge Questions 16, 17 and 29. HES recommendations regarding C-R functions for PM also affect recommendations on expert elicitation and alternatives to expert elicitation. Those recommendations will be discussed in response to Charge Question 29. The response to Charge Question 16 will address the cessation lag issue and the response to Charge Question 17 will address the question of alternative estimates

The Subcommittee agrees with EPA's current proposal to use cohort-based estimates in the base case. Different cohort studies and, within each study, various C-R functions are available, using different causes of death, exposure windows, subgroups, and models. The HES concludes that the base case should use the Pope et al. 2002 study, which relies on a larger number of deaths and longer follow-up of the American Cancer Society (ACS) cohort than does Pope et al. (1995) or its HEI reanalysis (Krewski et al., 2000). In addition, this analysis profited from the extensive experience and review process of Krewski et al. 2000, two of whose key authors (Krewski, Burnett) are also co-authors of Pope et al., 2002. The HES proposes that EPA use total mortality estimates. The cause specific estimates can be used to communicate the relative contribution of the main air pollution related causes of death. The HES, however, recommends that EPA not primarily use cause-specific estimates, given the larger uncertainties in these estimates. The estimates originate from a smaller number of cases with potential errors in coding of causes of death.

In the Analytical Plan, EPA makes good arguments for the use of the ACS cohort for the base case. However, the HES recommends modification in the way ACS and the Harvard 6-Cities Studies are compared (e.g., in Appendix D). ACS has some inherent deficiencies, in particular the imprecise exposure data, and the non-representative (albeit very large) population. Thus, ACS is not “the better study,” but, at this point in time, a prudent choice for the Second Prospective Analysis. The Harvard Six-Cities C-R functions are valid estimates on a more representative, although geographically selected, population, and its updated analysis has not yet been published. The Six Cities estimates may be used in a sensitivity analysis to demonstrate that with different but also plausible selection criteria for C-R functions, benefits may be considerably larger than suggested by the ACS study. The not yet published updated estimates of the expanded Harvard follow-up will be particularly useful for this purpose when they are accepted for publication in a peer-reviewed journal.

The Subcommittee had several discussions about the use of time-series based mortality functions. In line with published work on this issue, the HES would like to emphasize the

importance to understand and communicate the fundamental differences in the outcome of these studies as compared to cohort studies.

To estimate the full range of the contribution of air pollution to all processes that ultimately contribute to shortening in life expectancy one needs to follow large cohorts over many years to measure the association of the exposure experience with the person time in the population. ACS is an example of this approach. Although ACS published the data in the "case domain" (body counts), the underlying model uses person-year information (or survival time). Time series studies, on the other hand, estimate specifically the number of premature death affected by the exposure conditions shortly before death. The approach counts deaths rather than person-time, thus, it does not provide direct information about the lost time of life among these deaths. The Subcommittee therefore reminds the Agency that any assumption about the amount of time lost among these acute effect cases is a matter of judgment. The only information that can be derived from the time-series literature is the evidence that the lost time appears to be rather short (harvesting) for only a small fraction of the deaths.

Although cohort studies can be considered to measure the full range of person-time lost due to all kinds of effects of air pollution, this assumption is only theoretically true. Due to methodological limitations, the currently available cohort studies may most likely miss part of the time lost or the attributable cases (Kunzli, Medina et al., 2001; Martuzzi, 2001). Because of the limited amount of exposure data, these studies are unlikely to capture the mortality effects of specific short-term exposure patterns or the long term mortality consequences of exposures in early lifetime (unless the intra-city exposures in early life are highly correlated with those exposures measured primarily during middle age). The studies of early lifetime exposure suggest impaired lung function growth and accelerated decline in areas with higher pollution and strongly support the notion of chronic effects. Lung function is one of the strongest long-term predictors of life expectancy. Therefore, the findings on reduced lung function in children and adults are consistent with the shorter life expectancies as observed in the cohort studies.

The studies of long-term exposure may also fail to fully capture those deaths that lose only a short time period. The times-series approach has the advantage of capturing all deaths associated with short-term changes, regardless of the amount of lifetime lost. Thus, it is conceivable that the total air pollution-related death toll may be the sum of the cases derived from cohort studies plus some unknown fraction of those cases derived from time-series estimates. The overlap in these two quantities is not known. In addition, if there is non-differential exposure misclassification, it would likely lead to an underestimation of the effects. In the base case, the HES proposes that EPA assume full overlap, i.e. to ignore the additional short-term cases in the benefit analysis. In the sensitivity analysis or the expert elicitation, other probabilities of the overlap could be considered. However, the HES also suggests that mortality estimates based on the time-series studies alone be presented to inform the public of the implications of these studies. The advantage of these cases is that they reflect the portion of the problem that is expected to be resolved 'immediately' with improved air quality, whereas the uncertainty around lag time to full benefits is much larger for the chronic effect cases. Time-series studies with distributed lag models take this possibility into account and, thus, provide the C-R functions of choice to characterize the full range of short-term effects. However, these short-term estimates may utilize

recent evidence of stronger effects from cumulative exposure but should not be added to or substituted for the effects developed from the cohort studies.

The Subcommittee agrees that the interpretation of mortality risk results is enhanced if estimates of lost life years can be made. As mentioned, in contrast, time series studies do not provide direct estimates of the time lost although Burnett et al. (2003) has indicated that under certain restrictive assumptions, some conclusions can be drawn from these studies. Therefore, time lost among these acute cases cannot be readily derived and any assumptions on the average time lost remain a matter of judgment. The time lost may depend on the cause of death and the age at death. For example, whereas the acute terminal effects of air pollution on patients with lung cancer may make only a small change on life expectancy, a myocardial infarction in a 60 year old may lead to many years of life lost.

Different methods are available to estimate time lost among cohort-based cases of death. The Subcommittee proposes that EPA use life table approaches such as the one described by Miller and Hurley (2003). This paper applies estimates of relative risk to a given underlying population-at-risk and its associated age-specific death rates. The "static" approach takes the risk ratios from the cohort studies (i.e., the percentage change per unit PM2.5) and applies this to the baseline death rate to give “extra” deaths per year. Depending on the cause of death, it then estimates life years lost per death. This approach ignores how different death rates in any one year alter the population-at-risk in future years. Treating years as independent, it provides estimates of "extra deaths" or 'lives saved" each year. It seems that this is what EPA proposes.

The "dynamic" approach uses life-table methods to follow over time the impact on the population-at-risk of higher (lower) age-specific death rates. The consequent changes to the population-at-risk affect mortality estimates. These estimates are most naturally expressed in terms of earlier (later) deaths, i.e. in terms of changes in life expectancy or life-years lost. The observability of “extra death” has recently been questioned by Rabl (2003). The argument strongly depends on the assumptions of the underlying diseases processes. As mentioned by Rabl, "extra death" can be "observed" for chronic disease processes such as cancer. Lung cancer is part of the cohort mortality estimates. The Subcommittee agrees that the "cancer model" can be generalized to other long-term chronic disease processes of relevance in the air pollution domain. Thus, results can be expressed in terms of “extra” deaths or “saved” lives in various time-periods.

Which approach to use depends on: (a) correctness; (b) workability; and (c) whether the differences matter. On (a), the dynamic approach is more comprehensive, more correct, and pushes for greater transparency of assumptions. On (b), the static approach is easier to implement. However, the technical implementation issues of the life table approach are not difficult in principle and have been solved in practice. They need not be a deterrent to implementation. Workability also requires suitable economic valuation of an "extra" death or life-years lost, respectively. On (c), the two approaches give the same results for year 1. They diverge increasingly with time. This divergence, and its impact on mortality estimates, is positively associated with the size of the differences in hazard rates. The importance of the differences in mortality impacts is negatively associated with the discount rate used.

The Subcommittee recommends that: (a) whichever approach is used as primary, the other is used in a sensitivity analysis, and the results compared; (b) if differences are non-trivial, then the dynamic (life-table) approach be taken as best (Miller and Hurley 2003).

The Subcommittee also agrees that the whole range of uncertainties, such as the questions of causality, shape of C-R functions and thresholds, relative toxicity, years of life lost, cessation lag structure, cause of death, biologic pathways, or susceptibilities may be viewed differently for acute effects versus long-term effects.

For the studies of long-term exposure, the HES notes that Krewski et al. (2000) have conducted the most careful work on this issue. They report that the associations between PM2.5 and both all-cause and cardiopulmonary mortality were near linear within the relevant ranges, with no apparent threshold. Graphical analyses of these studies (Dockery et al., 1993, Figure 3 and Krewski et al., 2000, page 162) also suggest a continuum of effects down to lower levels. Therefore, it is reasonable for EPA to assume a no threshold model down to, at least, the low end of the concentrations reported in the studies.

Regarding the question of component relative toxicity, the evidence at this time supports differential toxicities based on particle chemistry is provided by a few studies of short-term exposure (e.g., Laden et al., 2000). Currently, there is little evidence from the long-term exposure studies to suggest differential toxicity. Therefore, it is prudent for EPA to assume equal toxicity across particle components and it is reasonable to explore alternative possible causes for differential particle component potency in supplementary sensitivity analyses.

Agency Charge Question 15: Alternative Analysis for PM Control

Charge Question 15. EPA estimates of benefit from particulate control may underestimate the impact of nonfatal cardiopulmonary events on premature mortality and life expectancy. For the base analyses, which rely on cohort evidence, the limited follow-up periods for the cohorts may not fully capture the impacts of nonfatal cardiovascular events on premature mortality later in life. For the alternative analyses –including cost-effectiveness analyses– which rely more on acute studies and life-expectancy loss, the years of life are estimated only for fatal events. Yet nonfatal events such as myocardial infarction reduce a person's life expectancy by a substantial percentage.

a. Do you agree that EPA, in the 812 analyses, should adjust benefit estimates to account for the mortality effects of non-fatal cardiovascular and respiratory events?
b. What medical studies and mathematical models of disease might be useful to review or use if EPA moves in this direction?
c. When the nonfatal events are valued in economic terms, should EPA assume that the published unit values for morbidity already account for the life-expectancy loss or should an explicit effort be made to monetize the resulting longevity losses?

HES Response: In regard to Question 15.a., a reasonable presumption to make is that the cohort mortality studies capture the full effect of PM on mortality and it would not be appropriate

to add additional mortality effects that might be associated with quantified PM morbidity effects such as nonfatal heart attack or chronic bronchitis. As noted above (see response Charge Question 14), some effects may be omitted in the cohort results. These omissions might be for those individuals with very short life expectancy (very short-term shift in timing of death), or those associated with very long term or distant past exposures (beyond the time frame of the cohort or due to increased measurement error from cohort member migration.

If short-term exposure mortality studies were to be used as the basis of mortality estimates *and* if the cohort study estimates were being ignored, then it would be appropriate to add mortality effects of PM-induced chronic illnesses. However, in response to charge question 14 above, the HES has strongly advised against ignoring the cohort study estimates.

The HES also discussed Quality Adjusted Life Year (QALY) estimates for cohort study-based mortality. The question is how the morbidity period that precedes death might be considered. The cohort study results do not tell us to what extent PM causes the ongoing disease that ultimately leads to death versus aggravating an already existing disease, but the HES sees from the morbidity studies that PM is a risk factor for onset of new chronic disease, at least for chronic bronchitis. Models of disease, as discussed for question 15.b. might be helpful in determining how to consider this. For some (uncertain) share of the deaths, PM is likely causing the disease as well as the death.

In regard to question 15.b., the HES notes: (a) that this is a conditional question (what medical studies and mathematical models of disease might be useful to review or use, if EPA moves in this direction) and (b) that, with use of the cohort studies, it is not necessary to move in this direction. Nevertheless, it is useful to consider the issue. The ideal basis for such estimates would be fully validated quantitative causal models of chronic cardiovascular and respiratory diseases, including contributions of air pollutants to both the chronic underlying disease processes, and acute events that precipitate clinical manifestations such as myocardial infarctions and arrhythmias associated with "sudden death." This ideal is not yet close to being realized. However, some data and models can contribute to the construction of reasonable preliminary assessments.

Some models can take the form of analogies with the prevention of fatal and nonfatal cardiovascular events by other types of interventions—for example pharmacological interventions such as cholesterol-lowering drugs. Long term double-blind intervention studies done for testing the efficacy and safety of these agents are the most secure basis for determining health improvements that are causally related to specific risk-factor-related interventions, although in some cases the length of follow-up may not be sufficient to provide ideal full-lifetime evaluations.

Longer follow-up is almost certainly possible by the use of long-term prospective epidemiological observations of the relationships between specific cardiovascular risk factors (e.g., fibrinogen levels, low FEV1 levels, low heart rate variability) and both total mortality and nonfatal cardiovascular and respiratory disease events. Such analogies may be considered promising as each of these three biomarkers has both associations with ambient airborne particle levels (Ackerman-Liebrich et al., 1997; Schwartz, 2001; Xu et al., 1991; Chestnut et al., 1991;

Pope et al., 1999; Gold et al., 2000 ) and significant independently predictive associations with cardiovascular mortality (Knuiman et al., 1999; James et al., 1999; Ryan et al., 1999; Lange et al., 1990; Folsom et al., 1997; Danesh et al., 1998; Huikuri et al., 1998; Tsuji et al., 1994; Klieger et al., 1987). To do these calculations, the long-term prospective cardiovascular epidemiology observations would be used to construct life table models to indicate the long-term changes in both non-fatal and fatal cardiovascular and respiratory events associated with specific amounts of change in each biomarker across the range of age groups studied. From these analogies, the amount of life shortening falling outside the follow-up limits of the air pollution cohort studies could be estimated, as well as effects from birth provided that: (1) migration is not too great, and (2) the pollution ranking of cities has not changed considerably over time.

In the Global Burden of Disease report (Ezzati et al., 2002), WHO utilized other techniques for estimating effects of chronic exposure prior to mortality. Therefore, HES also recommends that these methods be investigated.

In regard to question 15.c., (Do unit values for morbidity reflect life expectancy loss?), this will be further addressed by the Council, but in general, it depends on how the value estimate was derived. Cost-of-illness estimates include life expectancy losses (which are valued based on lost earnings/productivity) only if they are explicitly added. The values EPA is currently using for hospital admissions and for non-fatal heart attack do not include anything for life expectancy losses. Values for chronic bronchitis are based on a stated preference (willingness to pay) study (Viscusi et al., 1991). Lifetime symptoms of chronic bronchitis were described to respondents but nothing was mentioned about any potential reduced life expectancy.

Regarding the second part of Charge Question 15.c. (Should an explicit effort be made to monetize the resulting longevity losses?), actual longevity losses from chronic disease will be picked up by the cohort studies. If, as the HES advises, the cohort study estimates are always included, then it would not be right to incorporate the longevity losses also in the valuation of chronic disease.

Agency Charge Question 16. Cessation Lag

Charge Question 16. In recent EPA rulemakings, EPA's "base estimate" of benefit from PM control has been based on cohort epidemiological studies that characterize the chronic effects of pollution exposure on premature death as well as capturing a fraction of acute premature mortality effects. If these chronic effects occur only after repeated, long-term exposures, there could be a substantial latency period and associated cessation lag. As such, a proper benefits analysis must consider any time delay between reductions in exposure and reductions in mortality rates. For the acute effects, such as those considered in EPA's alternative benefit analyses, the delays between elevated exposure and death are short (less than two months), and thus time-preference adjustments are not necessary.

a. In the previous 812 analysis and in recent rulemakings, EPA assumed a weighted 5-year time course of benefits in which 25% of the PM-related mortality benefits were assumed to occur in the first and second year, and 16.7% were assumed to

occur in each of the remaining 3 years. Although this procedure was endorsed by SAB, the recent NAS report (2002) found "little justification" for a 5-year time course and recommended that a range of assumptions be made with associated probabilities for their plausibility. Do you agree with the NAS report that EPA should no longer use the deterministic, 5-year time course?

b. One alternative EPA is considering is to use a range of lag structures from 0 to 20-30 years, with the latter mentioned by NAS in reference to the Nyberg et al PM lung cancer study, with 10 or 15 years selected as the mid-point value until more definitive information becomes available. If this simple approach is used, should it be applied to the entire mortality association characterized in the cohort studies, or only to the difference between the larger mortality effect characterized in the cohort studies and the somewhat smaller effect found in the time series studies of acute exposure? Should judgmental probabilities be applied to different lags, as suggested by NAS?

c. Another option under consideration is to construct a 3-parameter Weibull probability distribution for the population mean duration of the PM mortality cessation lag. The Weibull distribution is commonly used to represent probabilities based on expert judgment, with the 3-parameter version allowing the shaping of the probability density function to match expected low, most likely, and expected high values. EPA is still considering appropriate values for the low, most likely, and expected high values –and therefore for the Weibull shape and location parameters– and EPA is interested in any advice the Council wishes to provide pertaining to the merits of this approach and/or reasonable values for the probability distribution.

HES Response: Given the purpose of the 812 Studies (to estimate a future situation), the time/lag is a very important issue. As noted by EPA, for short-term effects (including time-series based observations of mortality) this is not a problem, and there is even published evidence that these short-term effects closely follow changes in the pollution, thus, benefits are 'immediate' (on the annual aggregate level). For long-term effects, HES noted that empirical evidence is lacking to inform the choice of the lag distribution directly. This is because the cohort mortality studies reported to-date have lacked data on the long term time-course of exposures for each cohort member; such data, if available, might enable testing hypotheses regarding alternative exposure lag structures, if sufficient statistical power was available. Lacking direct information from the cohort studies themselves, new insights regarding the shape of the cessation lag can only come from improved mechanistic understanding of the chronic mortality exposure-response relationship. Information that may prove valuable in this regard could include results from clinical, experimental animal, and in-vitro studies, and analogies with the health effects of other long-term inhalation exposures, such as cigarette smoking. The clinical intervention literature (e.g., cardiovascular trials) or smoking cessation data may be useful.

The HES recommends that the Agency to derive models for each cause of death considered in the Second Prospective Study, as the lag structure most likely differs for different health problems. As a general rule, one may assume that the longer the air pollution sustained disease process is, the longer the delay. This may be true whether pollution is an initiator or a

promoter. For example, if inhalation of carcinogens from ambient air contributes to the incidence of lung cancer, the pathophysiologic process between exposure and death may take many years (for the average case) and the benefit of a 2000 to 2010 reduction in carcinogenic constituents in PM may lead to a reduction in lung cancer rates only after many years. For effects of long-term PM exposures on pulmonary disease (e.g., COPD), a useful model may be the change in the natural history of lung function with exposure to air pollution. Several studies are showing effects of long-term PM exposures on decreased lung function (Children's Health Study; Yale ISEE abstract 2002). By analogy with cigarette smoking, this may put people on steeper trajectories of lung function decline, which is a known risk factor for premature mortality. This might imply distributed lags extending over a substantial fraction of a lifetime. On the other extreme, some cardiovascular deaths captured in the cohort studies may be due to air pollution during the last months to years prior to death whereas the underlying susceptibility to a cardiovascular death may be due to non-air pollution causes (e.g. diabetes). Life time lost, captured in the cohort, may still be rather long (see above comments in response to Charge Questions 14.a. and 15). Clean air policies would bring a rather immediate benefit for such kind of cases. For example, Lightwood and Glantz (1997) conducted a meta-analysis of studies to determine how excess risks of myocardial infarction and stroke in smokers decline after quitting. They reported that risks would be reduced after roughly 1.5 years. Finally, to the extent that cohort results capture a portion of the acute time-series mortality effects of PM, there may be an even shorter lag.

EPA staff have presented several alternative lag structures, including the use of a flexible Weibull distribution spanning up to 25 years. It would be useful to utilize a distribution that could incorporate time lag to benefits based on three different patterns: purely acute effects based on exposure of 0-6 months, short-term cohort based on exposure of 2-5 years, and long-term cohort effects extending out 15-25 years. Thus, the HES supports either the use of a Weibull distribution or a simpler distributional form, such as uniform (made up of three segments to cover the three exposure periods outlined above), given our lack of knowledge on the form of the distributions. An important question to be resolved is what the relative magnitudes of these three components should be, and how much of the acute effects are assumed to be included in the cohort effect estimate. The Subcommittee suggests that if the three-segment uniform distribution is used, a smoother might be applied to the lag function to smooth the discontinuities. Given the current lack of direct data upon which to specify the lag function, HES recommends that this question be considered for inclusion in future expert elicitation efforts and/or sensitivity analyses. As noted, time lag to benefits may depend on the cause of death and the underlying morbidity processes that ultimately lead to premature death.

Agency Charge Question 17. Alternatives to the Base Estimate

Charge Question 17. In support of Clear Skies and several recent rule makings, the Agency has presented an Alternative Estimate of benefits as well as the Base Estimate. EPA developed the Alternative Estimate as an interim approach until the Agency completes a formal probabilistic analysis of benefits. NAS (2002) reinforced the need for a probabilistic analysis. The Alternative Estimate is not intended as a substitute method and needs to be considered in conjunction with the Base Estimate. Presentation of Base and Alternative estimates in the 812

Report may not be necessary if the probability analysis planned for the 812 Report is successful. While the Base Estimate assumes that acute and chronic mortality effects are causally related to pollution exposure, the Alternative Estimate assumes only acute effects occur or that any chronic effects are smaller than assumed in the Base Estimate. The Council's advice is sought on the following matters:

a. It has been noted by some particle scientists that the size of estimates based on time series studies that incorporate a distributed lag model, accounting for effects of 30 to 60 days after elevated exposure, may be similar in size to some interpretations of the results from the cohort studies. Does the Council agree that it is a reasonable alternative to use an estimate of the concentration-response function consistent with this view? If the Council agrees with the assumption, can it suggest an improved approach for use in an Alternative Estimate? The agency also seeks advice on appropriate bounds for a sensitivity analysis of the mortality estimate to be used in support of the Alternative Estimate.

b. An assumption that a specific proportion of the PM-related premature mortality incidences are incurred by people with pre-existing Chronic Obstructive Pulmonary Disease (COPD) and that these incidences are associated with a loss of six months of life, regardless of age at death. If these values are not valid, what values would be more appropriate? Do you recommend a sensitivity analysis of 1 to 14 years (with the latter based on standard life tables), as included in the draft regulatory impact analysis of the proposed Nonroad diesel rule?

c. An assumption that the non-COPD incidences of PM-related premature mortality are associated with a loss of five years of life, regardless of age at death. If these values are not valid, what values would be more appropriate? Do you recommend a sensitivity analysis of 1 to 14 years (with the latter based on standard life tables), as included in the draft regulatory impact analysis of the proposed Nonroad diesel rule?

d. Additional quantified and/or monetized effects are those presented as sensitivity analyses to the primary estimates or in addition to the primary estimates, but not included in the primary estimate of total monetized benefits. While no causal mechanism has been identified for chronic asthma and ozone exposure, there is suggestive epidemiological evidence.

1. Two studies suggest a statistical association between ozone and new onset asthma for two specific groups: children who spend a lot of time exercising outdoors and non-smoking men. We seek SAB comment on our approach to quantifying new onset asthma in the sensitivity analyses.
2. Premature mortality associated with ozone is not currently separately included in the primary analysis because the epidemiological evidence is not consistent. We seek SAB comment on our approach to quantifying ozone mortality in the sensitivity analyses.
3. Does the Council agree that there is enough data to support a separate set of

health impacts assessment for asthmatics? If so, does the approach proposed by the Agency address the uncertainty in the literature?

HES Response: In regard to question 17.a., the HES recommends that the alternative estimate be dropped from the Section 812 Analysis for several reasons. First, it gives a zero probability to the mortality effects of long-term exposure and in doing so, seriously underestimates the effects of air pollution. Second, there is little logic to providing a new low estimate without providing an accompanying new high estimate. As an alternative, the HES recommends that high and low estimates come from using the standard error around the existing C-R functions, including that using Pope et al., 2002 for premature mortality. The HES agrees with use of the cohort mortality studies for the base case estimate because this study design is capable of capturing effects of long-term PM exposure that the time series study design simply cannot capture. In the view of the HES, the selection process that EPA has used to develop the base case health estimates for PM provides a prudent estimate based on sound scientific evidence of effects. Although there is considerable uncertainty in the estimate for many reasons, it is not a worst-case estimate and it may be either higher or lower than the true effects. Therefore, the HES does not agree that the use of the time series mortality studies, adjusted for a distributed lag, is an acceptable single alternative estimate to the base case estimate.

In regard to questions 17.b. and c., which concern estimates of life-years lost, the HES notes that in the non-road diesel rule benefits assessment, life-years lost is calculated only in the alternative estimate, which is only for short-term exposure mortality. Causes of death are separated into COPD and non-COPD and in both cases, it is assumed that the affected individuals had serious pre-existing and life shortening chronic illness. This is a strong assumption (that everyone who dies from PM has severe pre-existing disease). Although it may be more defensible for the short-term exposure mortality (but even there it is probably too strong), it should not be applied to the mortality estimates based on cohort studies.

If the life-years lost calculations are going to be made for the short-term exposure mortality, the justification for the estimates of remaining life expectancy of 6 months (for COPD deaths) and 5-years (for non-COPD deaths) needs better documentation or at least discussion, especially for the assumption that it is invariant with age.

For calculating life-years lost for the cohort studies, the Subcommittee recommends contacting researchers using the ACS and the 6-cities data to see if they might have life-years lost estimates available based on their data. If not, the Subcommittee recommends staying with the life-years lost estimation procedure used in the first prospective analysis based on standard life tables. This assumes that in the absence of the PM exposure life expectancy would have been the same as the average for others of the same age and gender (which includes an average number of people with chronic disease). The first support for this assumption comes from the evidence presented in the ACS reanalysis showing that the mortality risk is no greater for those with pre-existing illness at the time of enrollment in the study (Krewski et al, 2000). The HES acknowledges, however, that uncertainties remain, given that no study has formally analysed the years of life lost and the dependence of years of life lost on causes of death, pre-existing diseases, and the underlying distributions of other susceptibilities.

In regard to question 17.d.i., which concerns methods for quantifying new onset asthma, the Subcommittee agrees that, so far, there are only two studies suggesting an effect of ozone on new onset (incidence) of asthma. Findings suggest some complex interactions of exposure and time-activity patterns outdoor, and the asthma literature indicates that onset of asthma depends on a variety of interacting factors, which may in addition change with age. Other air pollution studies are not conclusive on the issue. Thus, the HES proposes to disregard onset of asthma in the quantitative approach. The issue may be discussed qualitatively. The exclusion of this outcome may lead to some underestimation of the overall benefits.

Question 17.d.ii concerning ozone mortality is discussed later under question 30. In regard to question17.d.iii, concerning a separate asthma analysis, there is some appeal to looking at a subgroup that may have greater sensitivity to pollution exposure than the general population and those with asthma are a reasonable group to choose. However, with the recommendation that asthma exacerbation be added back into the primary set of C-R functions, the need for this is reduced.

Agency Charge Question 29: Plans for Expert Elicitation Pilot for Premature Mortality

Charge Question 29. Does the Council support the plans described in chapter 9 for the expert elicitation pilot project to develop a probability-based PM2.5 C-R function for premature mortality, including in particular the elicitation process design? If the Council does not support the expert elicitation pilot project, or any particular aspect of its design, are there alternative approaches the Council recommends for estimating PM-related mortality benefits for this analysis, including in particular a probabilistic distribution for the C-R function to reflect uncertainty in the overall C-R function and/or its components?

HES response: The HES supports the use of expert judgment as a means of systematically characterizing the state of knowledge about the likely health impacts of changes in PM2.5 concentrations. We fully endorse the view espoused by the recent National Research Council Committee on Estimating the Health Benefits of Air Pollution Regulations that the question is not whether expert judgment will be used, but how it will be used (National Research Council, 2002).

Expert judgments have long been important to risk assessment and management processes, because of the many uncertainties that need to be addressed. There are various approaches for incorporating expert judgment into risk assessment. These vary in many ways – including whether judgments are explicit or implicit, whether they are formally or informally elicited, whether (and the degree to which) they seek quantitative answers, and whether they seek consensus or not. It is well recognized that no single approach will suit all decision processes and that more formal approaches (which may be resource intensive) must be reserved for dealing with issues characterized by large uncertainty and substantial consequences of errors in decision making. The HES agrees with the Agency that the PM C-R mortality function is a good candidate for formal elicitation of expert judgment. While there have been several reviews of the use of formal expert judgment, little attention has been given to their potential application in support of environmental risk assessment (Wright and Ayton, 1994 and Walker, et al., 2001).

This pilot study presents a unique opportunity to thoughtfully examine the benefits and costs of this approach in such settings.

In any application of formally-elicited expert judgment, the major issues in the design of the study are:

a. definition of the question(s) to be elicited;
b. specification of the pool of relevant expertise and choice of an approach for identification and selection of experts;
c. determining which materials to include in a briefing book;
d. deciding whether to hold a workshop (at which the evidence can be reviewed; the procedures for eliciting expert judgment can be introduced; the protocol can be presented, discussed and revised; and at which the potential problems in eliciting judgments can be reviewed);
e. developing a protocol for eliciting judgments and determining:
    1. whether an aggregate question or a set of disaggregated questions will be used; and if a disaggregated approach is used,
        i. determining how to structure the questions, and
        ii. developing a method for dealing with correlated answers;
    2. what approaches will be used to encourage experts to fully consider the range of evidence, including contradictory evidence;
    3. whether elicitation aids (such as probability wheels) will be used;
f. determining whether efforts will be made to check the internal consistency of the judgments, and
g. deciding whether and how judgments will be combined, and if so, what information will be used in combining judgments (e.g., performance on calibration questions, peer or self ratings).

The HES review of the Agency's plans for the expert elicitation pilot project to develop a C-R function for PM related premature mortality has been particularly difficult because the materials available for review have been modified several times during the period of review. The original Analytic Plan was received in May and then in June (just days before the first scheduled Council and HES meeting) much of the key material relevant to the pilot study was withdrawn.

The initial HES evaluation of the plans was based a review of the brief (just over two-page) description of the Agency's plans available at the time of the 27-29 August HES meeting. These materials indicated that the Agency and its contractors were aware of the general literature in the field, and suggested that they were following generally accepted practice, but left the Subcommittee with many unanswered questions. These were described in a set of comments prepared by the HES after its 27-29 August public meeting and were provided to the Agency in draft form in a letter dated 21 October 2003. The HES concerns include the issues that follow.

Perhaps the most important question had to do with clear definition of the goal of the pilot project. Was it intended primarily to allow the Agency to gain experience with the formulation and conduct of expert judgment exercises? Or was it intended to provide information useful for

near-term policy analyses, such as the off-road diesel rule? The HES pointed out that our evaluation of the pilot study was heavily dependent on its intended purpose.

Secondly, HES members were concerned about the scope of the question to be addressed by the pilot expert judgment. Was the exercise intended to produce a concentration-response function for PM2.5 mass (without regard to source), or is it intended to address differential relative toxicity? Was the concentration-response function intended to represent the response averaged across the United States (without regard to background levels of PM2.5 and other pollutants), or was it intended to be applied to specific regions of the United States (allowing for background levels of PM2.5 and co-pollutants)? Were the results intended to be applied more broadly (e.g., outside of the United States)? Again, the HES indicated that advice about the utility of the approach taken and the results obtained would depend on knowing the answers to these questions.

Thirdly, the HES was not clear about the criteria that would be used in the selection of individual experts. The EPA had indicated that it was considering relying on experts selected from two recent National Academy of Science panels that had dealt extensively with airborne particulate matter and the HES agreed that this had certain merits, especially for the pilot study. However, the HES did not have adequate information to understand how the Agency intended to deal with the question of the disciplinary mix of experts involved in the study. The HES emphasized the need to use experts familiar with the elicited issues and to balance the group to ensure that experts from all key disciplines (epidemiology, toxicology, basic biology, clinical medicine) are well-represented. There was also some concern that attributes of the group other than discipline might need to be balanced as well. While recognizing that in the pilot project the number of experts must be limited, the HES urged the Agency to broaden the expert pool used in support of the final elicitations.

Fourth, the HES wondered why the Agency had decided to use a single composite (or aggregate) question – e.g., "What reduction in mortality would be expected from a 1 g/µ3 reduction in PM2.5 across the entire United States?"– rather than a set of disaggregated questions. This was in part because we worried that some analysts using the results might be frustrated if they could not understand the reasoning used by the experts to develop their characterizations of the state of knowledge. Many experts in the field argue that the quantitative answers are less important than the insights produced. In this spirit, the HES recommended that the Agency collect narrative descriptions of the rationale used by each expert and that these be presented along with the quantitative characterizations of uncertainty given by the experts. Further, the HES encouraged the Agency to rely on a disaggregated approach in the second stage of this work.

Fifth, on the basis of the limited materials available, the HES could not determine whether the experts would be engaged in the development of the elicitation protocol, briefing book and other materials. The HES noted that one of the most important determinants of the success of past exercises has been whether the experts involved had confidence in the process and argued that development of the briefing book and the elicitation protocol should involve an iterative process with extensive interaction between the experts and the elicitation team.

Sixth, the HES observed that the materials that had been provided were not clear about how the individual expert judgments would be aggregated. The HES advised the EPA to present first the entire collection of individual judgments, and then to follow the advice of Morgan and Henrion (1990). If the individual judgments are to be aggregated, the HES urged the EPA to present both simple (equal weight) aggregations and more complex (calibration weighted) versions of the results, and stressed that users of the information must be made aware of the entire spectrum of results.

Seventh, the original materials suggested that experts might be asked how to weight the results from time-series and cohort studies. The HES strongly disagreed with this approach; noted that cohort and time-series studies measure two different effects; and argued that they should be viewed as complementary sources of evidence, rather than as alternate sources of evidence. The HES urged the Agency to elicit both.

After the Agency provided the SAB Staff Office with the elicitation protocol for the pilot project to provide to the HES in late October, the HES discussed these issues at a public teleconference on 30 October 2003. The lead discussants relayed these views to the Council for further discussion at a public meeting on 5-6 November 2003. At that meeting, the Agency briefed the Council more completely on the approaches that it used in the selection and elicitation of experts. However, by the time the HES and Council received these materials, the pilot project was well-underway, the final elicitation protocol was complete, and many (if not all) of the expert elicitations had been conducted.

These materials provide answers to many of our original questions. For example, the elicitation protocol makes it quite clear that the Agency intends to use the results of the pilot project in the development of Regulatory Impact Assessments (RIAs) for specific proposed regulations (such as the non-road diesel rule and the PM transport rule). The protocol states that the elicitation will focus on determining the PM C-R function for specific changes in PM mass concentrations, and also indicates that auxiliary questions will be asked about the potential impact of PM composition. The Agency indicates that the five experts who participated in the elicitation, Jonathon Samet, Mark Utell, Bart Ostro, Roger McClellan and Scott Zeger, were selected on the basis of a process in which ten leading authors of PM mortality papers were asked to rank the members of the two relevant NAS panels. The protocol now includes several questions which ask experts to carefully outline the rationale underlying their stated judgments. The protocol clearly states that individual judgments (without specific attribution) and pooled results (using equal weights) will be provided as study results. The protocol asks experts to separately consider time-series and cohort evidence.

The HES is encouraged by these responses, but has a few residual concerns, including:

a. Whether the Agency believes that small pool of experts that could be studied in the pilot was adequate to reflect the legitimate spectrum of beliefs among experts from the several key disciplines? The HES recognizes that in order to make the pilot tractable it was necessary to limit participation, and is aware of the many factors which must be balanced in the selections of expert panels (Hawkins and Graham, 1988), but is concerned

about whether the judgments of such a limited group can reasonably be interpreted as representing a fair and balanced view of the current state of knowledge.

b. Whether the elicitation procedures ensured that experts would give adequate attention to contradictory evidence? While procedures may have been in place to cause experts to fully consider countervailing evidence and theory, neither the protocol nor the Agency briefing adequately described these.

c. Whether the approach used to deal with the relationships between evidence from time-series and cohort studies was fully adequate. While the HES believes that the approach reflected in the elicitation protocol is far superior to the Agency's original plan to ask the experts to weight the two approaches, the HES believes that further attention to the framing of the "short-term" and "long-term" effects of particulate matter may be appropriate. There is some concern among the HES that the definitions of "short-term" and "long-term" may have been somewhat ambiguous. Further, the HES believes that careful discussion of this framing during the review of the pilot project might lead to improvements in the design of subsequent expert elicitation studies.

d. Whether the decision to omit the workshop may have limited the ability of the experts to participate in the design of the protocol and thereby may have influenced their confidence in the process.

e. Whether the decision to ask the experts to use frequencies and probabilities in several different ways – e.g., response rates, subjective probabilities, percent reductions in response rates -- may have resulted in some confusion. The use of a single probability scale may be considered instead of the current variety of scales ranging from yes/no to (more informative) probability statements.

f. Whether there might have been benefits to using widely-available tools, such as probability wheels, in the elicitations. Two advantages of the approach used previously by Whitfield and Wallsten (1989) are that by relying on probability wheels response confusion is minimized and by asking each question in several different ways one may easily check for and assure consistency of responses.

However, in view of the fact that the pilot project is well-underway, the experts have already been selected, and many (if not all) of the interviews have been conducted, the HES sees little potential benefit in providing detailed suggestions about the design or conduct of the pilot study.

Instead, the HES focuses our comments on the review and interpretation of results from the pilot study. Specifically:

a. the HES recommends that the Agency conduct a thoughtful and comprehensive peer-review of the pilot study;

b. the HES recommends that the Agency view the results of the pilot study somewhat tentatively until the review is complete; and

c. the HES urges the Agency to apply a common sense standard to the results – i.e., do the experts involved "stand behind" the results? Do they believe that the process has faithfully captured their beliefs about the mortality effects of PM?

In summary, the HES generally supports the use of expert judgment to inform policy analysis; commends the EPA for moving in this direction; understands their hesitancy to move too quickly; supports the pilot study; questions whether it is advantageous to use the results of the pilot study in support of a major regulatory initiative; seeks much more detailed information about the approach used; advises that the process (but not the results) be subjected to careful peer review; and urges the EPA to invest adequate resources, time, and managerial attention to further development of this approach so that it can be used to inform this Second Prospective Analysis of the Clean Air Act.

Agency Charge Question 30: Plans for Estimating Independent Effects of Ozone Mortality

Charge Question 30. EPA plans to develop estimates of an independent mortality effect associated with ozone, as described in chapter 9. Does the Council support the use of the most recent literature on the relationship between short-term ozone exposure and daily death rates, specifically that portion of the literature describing models that control for potential confounding by PM2.5? Does the Council agree with the use of that literature as the basis for deriving quantified estimates of an independent mortality impact associated with ozone, especially in scenarios where short-term PM2.5 mortality estimates are used as the basis for quantifying PM mortality related benefits? Does the Council support the plans described in chapter 9 for the pilot project to use this literature to develop estimates of the ozone related premature mortality C-R function using the three alternative meta-analytic approaches? If the Council does not support this pilot project, or any particular aspect of its design, are there alternative approaches to quantifying ozone-related premature mortality that the Council recommends?

HES Response: Acute ozone effects pose an important yet complex issue that needs to be addressed as EPA moves forward with benefits analyses. A large and growing literature exists on ozone mortality associations with and without control of PM covariates. However, the interpretation of these results is made complicated by several issues, including possible confounding by PM, effect modification by season and interactions with temperature and other weather factors. Thus, the effects are hard to ignore, but their interpretation remains problematic, raising questions as to how best to incorporate these effects into the benefits analysis. The Subcommittee endorses EPA's plans to sponsor three new meta-analyses of ozone impacts. This will yield information on the consistency of the effects of ozone and to what extent they are independent of PM. While the HES agrees with EPA that PM2.5 is the most important co-pollutant to be concerned about, the meta-analyses should not necessarily be limited to only those ozone studies that have PM2.5 data. Other studies may also be informative, including those using PM10, estimated PM2.5, and/or optical measures of blackness. The Subcommittee looks forward to reviewing the results of these meta-analyses.

Agency Charge Question 32: Evaluating Data Quality and Plans for Publication of Intermediate Data Products

Agency Charge Question 32. Does the Council support the plans described in chapter 10 for evaluating the quality of data inputs and analytical outputs associated with this study, including the planned publication of intermediate data products and comparison of intermediate and final results with other data or estimates? If the Council does not support these plans, are there alternative approaches, intermediate data products, data or model comparisons, or other data quality criteria the Council recommends? Please consider EPA's Information Quality Guidelines in this regard.

HES Response: The Subcommittee enthusiastically supports EPA's plan to make available through EPA's web site the intermediate information and data products produced in the course of the 812 analysis. The BENMAP system demonstrated to the Subcommittee appears to be an invaluable tool for both generation and facilitation of a widespread understanding of the analysis and its results. In particular, it will enhance understanding of the assumptions used in constructing the aggregates of results, and the consequences of alternative aggregation approaches and assumptions.

It might be of interest to assess the degree of "surprise"—where possible compare the extent of each change with the prior belief about the uncertainty in the estimate. Historically, even in fields with well established procedures for estimating uncertainties (such as measurements of elementary particle masses by physicists), it is found that traditional statistical procedures for estimating standard errors, etc. systematically understate actual uncertainties as later calculated by comparing improved measurements with older measurements and previously estimated uncertainties (for examples see the references provided below). This is because traditional statistical uncertainty estimation approaches tend to be based solely on random sampling-error uncertainties in the data, neglecting what frequently turns out to be appreciable systematic or calibration errors (Shlyakhter 1992, 1994a and 1994b). Developing fair estimates of uncertainties for the CAAA benefit and cost projections will require analysts to have inputs that can be interpreted in terms of both types of uncertainty. Systematic evaluation of the extent and reasons for changes in successive sets of emissions estimates will be a start toward providing invaluable inputs to the overall uncertainty analysis.

The HES also suggests that there is some value in having clearly stated data quality objectives (DQOs) and a specific comprehensive data quality assurance (QA) protocol. These objectives should be derived from the context of the 812 Analysis and should guide the design and presentation of the intermediate data products to best serve the needs of specific audiences for the data. Discussion among the group identified two broad types of users whose differing needs should be kept in mind: (a) policy and staff advisors whose main goal may be to understand the basis of the 812 analysis and its conclusions, and (2) analysts who wish to conduct independent evaluations based on data used by the Agency. With the needs of these two groups in mind, the disclosure and ready availability of the intermediate data products, presented on the website and otherwise in context along with a summary of the DQOs, should greatly enhance the value of the 812 analysis for both public and private sector decision-makers.

Agency Charge Question 33: Plans for aggregation and presentation of analytical results from the Health Analysis

Charge Question 33: Does the Council support the plans described in Chapter 11 for the aggregation and presentation of analytical results from this study? If the Council does not support these plans, are there alternative approaches, aggregation methods, results presentation techniques, or other tools the Council recommends?

HES Response: For the first prospective study, EPA compared costs to benefits for the years 2000 and 2010. The Agency also aggregated the net present value of costs and benefits for the 1990 through 2010 period. The approach was to use a linear interpolation between the years 1990 and 2000 and a second linear interpolation between 2000 and 2010. The linear interpolation was used because air quality modeling was only carried out for the years 2000 and 2010.

The modeling results for the first study supported estimates of annual and cumulative costs for Titles I through V and annual estimates for Title VI. The benefits were not disaggregated by Title nor, with some minor exceptions, were they disaggregated by geographic area, although spatially disaggregated data were presented in the report appendices.

a. Alternative approaches: The formal probability analysis method will eventually be used to provide better estimates of uncertainty and estimations of model sensitivity to modeled factors. This may be superior to the use of comparing results of applying different analytical methodologies to assess uncertainty.

b. Aggregation methods: There are only a few C-R functions for source-specific health effects and therefore limited information for sector specific PM health benefits or for apportioning health benefits among sources or sectors other than as a function of source-specific contributions to ambient PM mass. With the exception of particle size considerations, the toxicity of all PM is treated as equivalent regardless of its origin. There is limited evidence (i.e., Laden et. Al., 2000) to suggest some differential toxicity of PM, at least regarding mortality and daily PM exposures. If the data are available on source-specific changes in PM, EPA should consider conducting a limited sensitivity analysis utilizing some of this evidence.

1. Sectoral Disaggregation – The plan for generating sector-specific benefit results involves independent scenarios that selectively omit emissions reductions for a single sector (i.e. holding emissions at pre-CAAA levels) while bringing all other sectors to their post-CAAA levels. The Air Quality Modeling Subcommittee has evaluated the issues of emissions estimates and transport. The HES assumes the estimates will include data to compute exposures to both fine and coarse mode particles. The Agency can use these exposures in conjunction with appropriate C-R functions to estimate health benefits by sector.

2. Spatial Disaggregation – The cost and benefit modeling for spatial disaggregation

will be presented in the Appendix. There are limitations in ability to predict population growth patterns on a spatial level over several years accurately. Also on a regional level, areas that incur pollutant abatement costs may be different from areas that receive health benefits. Spatially disaggregated health benefits can be estimated but because of the mismatch with costs, it may be difficult to interpret the disaggregated net benefits.

3. Pollutant Endpoint Disaggregation – In cases where endpoint-pollutant combinations can be identified that can be associated with a specific benefit, disaggregated benefits can be presented. Detailed statistical analyses to identify pollutant interactions have been used in apportioning air pollution contributions among sources. It may be possible to use such source-receptor methods for disaggregating health effects among pollutant combinations.

Agency Charge Question 34: Plans for Stratospheric Ozone Analysis

Charge Question 34. Does the Council support the plans describe in Appendix E for updating the estimated costs and benefits of Title VI programs? If the Council does not support these plans, are there alternative data, models, or methods the Council recommends?

HES Response: The proposed revised approach to determining costs and benefits of controls to limit stratospheric ozone reductions by anthropogenic chemicals is sound, and addresses the issue comprehensively. Recent advances in knowledge and models make it possible to address the issue with somewhat greater confidence, while still recognizing that great uncertainties remain concerning both scientific and economic assumptions and constraints when dealing with a time frame extending to 2075. Overall, the Subcommittee concludes that the plans make quite reasonable assumptions and choices.

The Subcommittee suggests that the text be revised to provide more information on two points: (a) the basis for the effects coefficient for cataract formation, and (b) the basis for the effects coefficient for basal cell carcinoma and malignant melanoma. The Subcommittee also suggests the following specific comments to strengthen Appendix E: (a) on page E-4, the judgment that unquantified ecological benefits are minimal compared to the benefits estimated by the AHEF model could be correct, but needs to be better justified, and (b) on page E-6, replace "ozone depletion" with the term "ODS control". Additionally, the text needs to clarify the source of the cataract data to be used (in the public meeting, EPA staff said it was the National Eye Institute database) and any sample size or other issues with the data that would raise concerns about its use for this analysis. Although the state of the science is not well developed, the levels of uncertainty in both the cancer and cataract data need to be described and their potential impacts on the cost-benefit analysis discussed. Mention of the limitations and/or lack of data from animal models relevant to specific human outcomes (e.g., basal cell carcinoma, malignant melanoma, etc.) would strengthen this section.

Agency Charge Question 35: Plans for an Air Toxic Case Study

Charge Question 35. Does the Council support the plans described in Appendix E for the benzene case study, including the planned specific data, models, and methods, and the ways in which these elements have been integrated? If the Council does not support these plans, are there alternative data, models, or methods the Council recommends?

HES Response: The Subcommittee notes that the basic conception of the case study is reasonable, given that the chemical chosen is data rich, and therefore not a typical air toxic. Several suggestions for strengthening the approach follow. The plan for deriving the C-R function mentions only an analysis of a relatively small (only nine leukemia cases) and older epidemiology study (Crump et al., 1994). The current plan neglects much newer and more extensive leukemia and supporting chromosome breakage, and other genetic biomarker exposure response data collected by U.S. researchers among large numbers of Chinese workers with a broad range of exposures (Hayes et al., 2000, 1997; Rothman et al., 1995, 1996a, 1996b, 1997.) The exposure estimates used in these studies have been criticized (Wong, 1999), however further work with the authors of the study seems likely to be able to produce dose response information that is at least equal to, and likely superior to, that which is the basis of the older benzene cancer potency estimates. One particularly important implication of the newer information is that in contrast to the suggestion of an upward turning curve from the older higher dose data, the newer data seem to indicate a convex dose response shape (linear at low doses, with some flattening at higher dose rates). This finding is consistent with high dose saturation of the generation of some genetically active activated intermediate metabolite, most likely a metabolite produced by a specific P450 enzyme (Rothman et al., 1997).

The HES also suggests that EPA consider and reviews other well-conducted studies, especially where these have been conducted at exposure levels closer to what the general public may experience (e.g. Rushton and Romaniuk (1997); OEM: 54,152-166; and Schnatter et al. (1996); OEM: 53, 773-781). Uncertainty assessment should include consideration of extrapolation from high-exposure studies of adult (usually male) workers, to the lower exposures and more diverse population of the public.

In regard to the data, the 1990 data, measured by Texas Natural Resource Conservation Commission, will be used as the base case (pre-CAAA). The 1999 NTI could be used as a surrogate for the 2000 (post-CAAA) data. The Agency, might, however, find it more consistent to project the data to 2000. The HES considered the four options identified by the Agency for incorporating CAAA impacts. Option 2 takes into account MACT expectations as well as impact of the Houston Ozone State Implementation Plan (SIP) provisions, but Option 3, which uses existing EPA databases, might be easier to implement.

The plan to limit the case study to the Houston area makes sense for this first cut. If the benefits turn out to be non-negligible, a broader application of the case study might be warranted. Extension to Portland and/or Philadelphia should depend on the Houston outcome.

Agency Charge Question 36. A cessation lag for benzene-induced leukemia is difficult to estimate and model precisely due to data limitations, and EPA plans to incorporate a five-year cessation lag as an approximation based on available data on the latency period of leukemia and

on the exposure lags used in risk models for the Pliofilm cohort (Crump, 1994 and Silver et al., 2002). Does the SAB support adoption of this assumed cessation lag? If the Council does not support the assumed five-year cessation lag, are there alternative lag structures or approaches the Council recommends?

HES Response: The simple lag interpretation of 5 years mentioned in the blueprint does not seem to utilize all the material in the original Crump (1994) paper--in particular, an equation (utilizing the parameter K) that Crump uses to weight exposures that occurred at different times relative to the appearance of the leukemias. Some finite minimum lag is likely to be justified by the growth rate of tumors from initial single cells to the point at which there are enough cells to be clinically detectable as a cancer. This issue needs to be revisited in the light of a more recent analysis of data from the original U.S. cohort (Silver et al., 2002) as well as observations of the distributions of excess tumors in studies of radiation-induced leukemias. If available, data from the NCI-Chinese studies (cited above) should also be analyzed for differences in the timing of exposures and the timing of the appearance of tumors.

# REFERENCES

Ackermann-Liebrich, U, et al. 1997. Lung Function and Long Term Exposure to Air Pollutants in Switzerland. *Am. J. Respir. Crit. Care Med*. 155, 122-129.

Belanger, K., Beckett, W., Triche, E., Bracken, M.B., Holford, T., Ren, P.., McSharry, J.E., Gold, D.R., Platts-Mills, T.A., Leaderer, B.P. 2003. Symptoms of wheeze and persistent cough in the first year of life: associations with indoor allergens, air contaminants, and maternal history of asthma. *Am J Epidemiol*. 158:195-202.

Brunekreef et al. 1997. Air Pollution from Truck Traffic and Lung Function in Children Living Near Motorways. *Epidemiology* 8: 298-303.

Burnett, R T., Smith-Doiron, M., Stieb, D., Raizenne, M.E., Brook, J.R., Dales, R.E., Leech, J.A., Cakmak, S., Krewski. D. 2001. Association between ozone and hospitalization for acute respiratory diseases in children less than 2 years of age. *Am. J. Epidemiol*. 153: 444-452.

Chay, K.Y., Greenstone, M. 2001. The impact of air pollution on infant mortality: Evidence from geographic variation in pollution shocks induced by a recession. Berkeley, CA: University of California, Berkeley, Department of Economics. Available: http://elsa.berkeley.edu/users/kenchay/].

Chestnut, L. G., Schwartz, J, Savitz, D, Burchfiel, C. M. 1991. Pulmonary Function and Ambient Particulate Matter Epidemiological Evidence from NHANES I. *Arch. Environ. Health* 46(3), 135-144.

Clancy, L., P. Goodman, et al. 2002. Effect of air-pollution control on death rates in Dublin, Ireland: an intervention study. *Lancet* 360(9341): 1210-4.

Cooke, RM. 1991. *Experts in Uncertainty: Opinion and Subjective Probability in Science*. Oxford University Press, New York.

Crump, K. S. 1994. Risk of benzene-induced leukemia: A sensitivity analysis of the pliofilm cohort with additional follow-up and new exposure estimates. *J. Toxicol. Environmental Health* 42: 219-242.

Danesh, J., Collins, R. Appleby, P., Peto, R. 1998. Association of Fibrinogen, C-reactive Protein, Albumin, or Leukocyte Count with Coronary Heart Disease. JAMA, V. 279, #18, p. 1477-82.

Dockery, D.W., Pope, C.A. III, Xu, X., Spengler,, J.D., Ware, J.H., Fay, M.E .et al. 1993. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 329:1753-9.

Dominici, F., A. McDermott, et al. 2003. Airborne particulate matter and mortality: timescale effects in four US cities. *Am J Epidemiol* 157(12): 1055-65.

Ezzati M., Lopez, A.D., Rodgers A., et al. 2002. Selected major risk factors and global and regional burden of disease. *Lancet* 360: 1347-60.

Folsom, A. R., Wu, K. K., Rosamond, W. D., Sharrett, A. R., and Chambless, L. E.. 1997, "Prospective study of hemostatic factors and incidence of coron*ary* heart disease.. The Atherosclerosis Risk in Communities (ARIC) study. *Circulation* v. 96, p. 1102-1108.

Gilliland, F.D., Berhane, K., Rappaport, E.B., Thomas, D.C., Avo,l E., Gauderman ,W..J, London, S.J., Margolis, H.G., McConnell, R., Islam, K.T., Peters, J.M. 2001 The effects of ambient air pollution on school absenteeism due to respiratory illnesses. *Epidemiol.* 12:43-54

Gold, D.R., Litonjua, A. Schwartz, J., Lovett, E., Larson, A., Nearing, B., Allen, G., Verrier, M., Cherry, R., Verrier, R. 2000. Ambient Pollution and Heart Rate Variability. *Circulation,* v. 101, p.1267-73.

Hattis, D. and Burmaster, D. E. 1994. Assessment of Variability and Uncertainty Distributions for Practical Risk Analyses. *Risk Analysis,* 14: 713-730.

Hattis, D., Russ, A., Goble, R., Banati, P., and Chu, M. 2001. Human Interindividual Variability in Susceptibility to Airborne Particles. *Risk Analysis*, Vol. 21(4), pp. 585-599.

Hawkins NC and Graham JD. 1988. Expert scientific judgment and cancer risk assessment: a pilot study of pharmacokinetic data. *Risk Analysis,* 8, 615-625.

Hayes, R. B., Yin, S., Rothman, N., Dosemeci, M., Li, G., Travis, L. T., Smith, M. T., and Linet, M. S. 2000. Benzene and lymphohematopoietic malignancies in China. *J. Toxicol. Environ. Health A.* 61: 419-432.

Hayes, R. B., Yin, S. N., Dosemeci, M., Li, G. L., Wacholder, S., Travis, L. B., Li, C. Y., Rothman, N., Hoover, R. N., and Linet, M. 1997. Benzene and the dose-related incidence of hematologic neoplasms in China . *J. Nat. Cancer Institute* 89: 1065-1071.

Hoek, G., Brunekreef, B., Verhoeff, A., van Wijnen, J., Fischer, P. 2000. Daily mortality and air pollution in The Netherlands. *J Air Waste Manag Assoc* 50(8):1380-9.

Hoek, G., Brunekreef, B., Fischer, P., van Wijnen, J. 2001. The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. *Epidemiology* 12(3):355-7.

Hoek, G., B. Brunekreef, et al. 2002. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. *Lancet* 360(9341): 1203-9.

Huikuri, H.V., et al. 1998. Power-Law Relationship of Heart Rate Variability as a Predictor of Mortality in the Elderly. *Circulation* 97, 2031-2036.

Kleiger, R. E., Miller, J. P., Bigger, J. T., Moss, A. J., and the Multicenter Post-Infarction Research Group. 1987. Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. *Am. J. Cardio*l , v. 59, p. 256-262.

Kaiser R., Künzli N., Schwartz J. 2001. The impact of PM10 on infant mortality in 8 US cities.

*Am J Respir Crit Care Med*. 163(5):A881.

Krewski, D,, Burnett, R., Goldberg, M.S., Koover, K., Siemiatycki, J., Jerrett, M. et al. 2000. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. *Res Rep Health Eff Inst (A special report of the Institute's Particle Epidemiology Reanalysis Project)*.

Kunzli, N., S. Medina, et al. 2001. Assessment of deaths attributable to air pollution: should we use risk estimates based on time series or on cohort studies? *Am J Epidemiol* 153(11): 1050-5.

James, A. L., Knuiman, M.W., Divitini, M.L., Musk, A. W, Ryan, G., Bartholomew, H.C. 1999. Associations Between White Blood Cell Count, Lung Function, Respiratory Illness and Mortality: the Busselton Health Study. *Eur. Respir. J.* 13, 1115-1119.

Knuiman, M. W., James, A. L., Divitini, M. L., Ryan, G., Bartholomew, H. C., Musk, A. W. 1999. Lung Function, Respiratory Symptoms, and Mortality: Results from the Busselton Health Study. *Ann. Epidemiol.* 9, 297-306.

Laden, F., L. M. Neas, et al. 2000. Association of fine particulate matter from different sources with daily mortality in six U.S. cities. *Environ Health Perspect* 108(10): 941-7.

Lange, P., Nyboe, J., Appleyard, M., Jensen, G., Schnohr, P. 1990 Spirometric Findings and Mortality in Never-Smokers. *J. Clin. Epidemiol.* 43, 867-873.

Lightwood, J.M. and Glantz, S.A. 1997 Short-term economic and health benefits of smoking cessation. Myocardial infarction and stroke. *Circulat*ion 96, 1089-1096.

Lippmann, M., Frampton, M., Schwartz, J., Dockery, D., Schlesinger, R.B., Koutrakis, P., Froines, J., et al. 2003. The U.S. Environmental Protection Agency particulate matter health effects research centers program: A midcourse report of status, progress, and plans. *Environ. Health Perspect.* 111:1074-1092.

Lippmann, M,, Ito, K,, Nadas, A,, Burnett, R.T. 2000. Association of particulate matter components with daily mortality and morbidity in urban populations. *Res Rep Health Eff Inst* (95):5-72, discussion 73-82.

Lipfert, F.W., Zhang, J., Wyzga, R.E. 2000. Infant mortality and air pollution: A comprehensive analysis of U.S. data for 1990. *J. Air Waste Manage. Assoc*. 50:1350-1366.

Martuzzi, M. 2001. "Re: "Assessment of deaths attributable to air pollution: should we use risk estimates based on time series or on cohort studies?" *Am J Epidemiol* 154(10): 974-5.

Miller, B. G. and J. F. Hurley. 2003. Life table methods for quantitative impact assessments in chronic mortality. *J Epidemiol Community Health* 57(3): 200-6.

Moolgavkar, S.H. 2000.. Air Pollution and Hospital Admissions for Diseases of the Circulatory

System in Three U.S. Metropolitan Areas. *J Air Waste Manag Assoc* 50:1199-206.

Morgan, MG and Henrion, M. 1990. *Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis*. Cambridge University Press, Cambridge, UK

National Research Council. 2002. *Estimating the Public Health Benefits of Proposed Air Pollution Regulations.* National Academy Press, Washington, DC.

Nyberg, F., P. Gustavsson, et al. 2000. Urban air pollution and lung cancer in Stockholm. *Epidemiology* 11(5): 487-95.

Pope, C. A. I. 1996. Particulate pollution and health: a review of the Utah valley experience. *J Exp Anal Environ Epidemio*l 6(1): 23-34.

Pope, C.A. III, Burnett, R.T., Thun, M..J, Calle, E.E., Krewski, D., Ito, K., Thurston, G.D. 2002. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 287:1132–1141

Pope, C.A. III, Thun, M.J., Namboodiri, M.M., Dockery, D.W., Evans, J.S., Speizer, F.E. et al. 1995. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. *Am J Respir Crit Care Med* 151:669-74.

Pope, C.A., Verrier, R.L., Lovett, E.G., Larson, A.C., Raizenne, M.E., Kanner, R.E., Schwartz, J., Villegas, G.M., Gold, D.R., Dockery, D.W. 1999. Heart rate variability associated with particulate air pollution. *American Heart Journal,* v. 138, #5, p. 890-9.

Rabl A. 2003. Interpretation of air pollution mortality: number of deaths or years of life lost? *J Air Waste Manag Assoc* 53:41-50.

Rothman, N., Haas, R., Hayes, R. B., Li, G. L., Wiemels, J., Campleman, S., Quintana, P. J. E., Xi, L. J., Dosemeci, M., Titenko-Holland, N., Meyer, K. G., Lu, W., Zhang, L. P., Bechtold, W., Wang, Y. Z., Kolachana, P., Yin. S. N., Blot, W., and Smith, M. T. 1995. *Proc. National Acad. Sci.* 92: 4069-4073.

Rothman, N., Smith, M. T., Hayes, R. B., Li, G. L., Irons, R. D., Dosemeci, M., Haas, R., Stillman, W. S., Linet, M., Xi, L., Bechtold, W. E., Wiemels, J., Campleman, S., Zhang, L., Quintana, P. J. E., Titenko-Holland, N., Wang, Y. Z., Lu, W., Kolachana, P., Meyer, K. B., and Yin, S. 1996. An epidemiologic study of early biologic effects of benzene in Chinese workers. *Environmental Health Perspectives* 104 (Suppl. 6): 1365-1370.

Rothman, N., Li, G. L., Dosemeci, M., Bechtold, W. E., Marti, G. E., Wang, Y. Z., Linet, M., Xi, L., Lu, W., Smith, M. T., Titenko-Holland, N., Zhang, L., Blot, W., Yin, S., and Hayes, R. B. 1996. Hematotoxicity among Chinese workers heavily exposed to benzene. *American J. Indust. Med.* 29: 236-246.

Rothman, N., Smith, M. T., Hayes, R. B., Traver, R. D., Hoener, B., Campleman, S., Li, G. L., Dosemeci, M., Linet, M., Zhang, L., Xi, L., Wacholder, S., Lu, W., Meyer, K. B., Titenko-Holland, N., Stewart, J. T., Yin, S., and Ross, D. 1997. Benzene poisoning, a risk factor for hematological malignancy, is associated with the NQ01 609C□T mutation for rapid fractional excretion of chlorzoxazone. *Cancer Research* 57: 2839-2842.

Rushton, L. and Romaniuk, H. 1997. A case-control study to investigate the risk of leukaemia

associated with exposure to benzene in petroleum marketing and distribution workers in the United Kingdom. *Occupational and Environmental Medicin*e 54: 152-166 (Abstract on http://oem.bmjjournals.com/cgi/content/abstract/54/3/152).

Ryan, G. et al. 1999. Decline in Lung Function and Mortality: The Busselton Health Study. *J. Epidemiol. Community Health* 53, 230-234.

Samet. J.M., Zeger, S.L., Dominici, F., Curriero, F., Coursac, I., Dockery, D.W. et al. 2000a. The National Morbidity, Mortality, and Air Pollution Study. Part II: Morbidity and mortality from air pollution in the United States. *Res Rep Health Eff Inst* (94 Pt 2):5-70; discussion 71-9.

Schnatter, AR et al. 1996. Lymphohaematopoietic malignancies and quantitative estimates of exposure to benzene in Canadian petroleum distribution workers. *Occupational and Environmental Medicine* 53: 773-781. Abstract on http://oem.bmjjournals.com/cgi/content/abstract/53/11/773

Schwartz, Joel. 2001. Air Pollution and Blood Markers of Cardiovascular Risk. *Env. Health Persp.* V. 109, supplement 3, p. 405-9.

Shlyakhter, A. I., and Kammen, D. M. 1992. Sea-Level Rise or Fall? *Nature* 253:25.

Shlyakhter, A.I. 1994A. An Improved Framework for Uncertainty Analysis: Accounting for Unsuspected Errors. Risk Analysis 14:441-447.

Shlyakhter, A.I. 1994B Uncertainty Estimates in Scientific Models: Lessons from Trends in Physical Measurements, Population and Energy Projections. In *Uncertainty Modeling and Analysis: Theory and Application,* B. M. Ayyub and M. M. Gupta, Eds., Elseiver Science, B. V., 1994, pp. 477-496.

Silver, S. R., Rinsky, R. A., Cooper, S. P., Hornung, R. W., and Lai, D. 2002. Effect of follow-up time on risk estimates: A longitudinal examination of the relative risks of leukemia and multiple myeloma in a rubber hydrochloride cohort. *American J. Ind. Med*. 42: 481-489.

Smith, M. T., Zhang, L., Wang, Y., Hayes, R. B., Li, G., Wiemels, J., Dosemeci, M., Titenko-Holland, N., Xi, L., Kolachana, P., Yin, S., and Rothman, N. 1998. Increased translocations and aneusomy in chromosome 8 and 21 among workers exposed to benzene. *Cancer Research* 58: 2176-2181.

Sorlie, P., W. Kannel, et al. 1989. Mortality associated with respiratory function and symptoms in advanced age; The Framingham Study. *Am Rev Respir Dis* 140: 379-84.

Tsuji, H., Venditti, F.J., Manders, E.S., Evans, J.C., Larson, M.G., Feldman, C.L., Levy. D. 1994. Reduced Heart Rate Variability and Mortality Risk in an Elderly Cohort: The Framingham Heart Study. *Circulation*, V. 90, p. 878-83, August 1994.

Venn, A. J., S. A. Lewis, et al. 2001. Living near a main road and the risk of wheezing illness in children. *Am J Respir Crit Care Med* 164(12): 2177-80.

Walker KD, Evans JS, and MacIntosh D. 2001. Use of expert judgment in exposure assessment.

PartI. Characterization of personal exposure to benzene. *Risk Analysis*. 11:308-322.

Whitfield RG and Wallsten, TS. 1989. A risk assessment for selected lead-induced health effects: an example of a general methodology. *Risk Analysi*s, 9, 197-207.

Wong, O. 1999. A critique of the exposure assessment in the epidemiologic study of benzene-exposed workers in China conducted by the Chinese Academy of Preventive Medicine and the U. S. National Cancer Institute. *Regulatory Toxicolgoy and Pharmacology* 30: 259-267.

Woodruff, T.J., Grillo, J., Schoendorf, K.C. 1997. The relationship between selected causes of postneonatal infant mortality and particulate air pollution in the United States. *Environ. Health Perspect.* 105:608-612.

*Wright GW and Ayton P. (eds.) 1994. Subjective Probability.* John Wiley and Sons. New York, NY.

Xu. X., Dockery D. W., and Wang, L.. 1991. Effects of Air Pollution on Adult Pulmonary Function. *Arch. Environ. Health* 46(4), 198-206 .

Zhu, Y., Hinds, W.C., Kim, S., Sioutas, C. 2002. Concentration and size distribution of ultrafine particles near a major highway. *J Air Waste Manage* 52:1032-1042.

# APPENDIX A
# List of Charge Questions Provided to the HES

Listed below are the charge questions addressed by the Health Effects Subcommittee of the Advisory Council in Clean Air Compliance Analysis in this report.

Charge Question 11. Does the Council support the plans described in chapter 6 for estimating, evaluating, and reporting changes in health effect outcomes between scenarios? If there are particular elements of these plans which the Council does not support, are there alternative data or methods the Council recommends?

Charge Question 12. EPA seeks advice from the Council regarding the technical and scientific merits of incorporating several new or revised endpoint treatments in the current analysis. These health effect endpoints include:

a. Premature mortality from particulate matter in adults 30 and over, PM (Krewski et al., 2000);
b. A PM premature mortality supplemental calculation for adults 30 and over using the Pope 2002 ACS follow-up study with regional controls;
c. Hospital admissions for all cardiovascular causes in adults 20-64, PM (Moolgavkar et al., 2000);
d. ER visits for asthma in children 0-18, PM (Norris et al., 1999);
e. Non-fatal heart attacks, adults over 30, PM (Peters et al., 2001);
f. School loss days, Ozone (Gilliland et al., 2001; Chen et al., 2000);
g. Hospital admissions for all respiratory causes in children under 2, Ozone (Burnett et al., 2001); and,
h. Revised sources for concentration-response functions for hospital admission for pneumonia, COPD, and total cardiovascular: Samet et al., 2000 (a PM10 study), to Lippmann et al., 2000 and Moolgavkar, 2000 (PM2.5 studies).

Charge Question 13. EPA seeks advice from the Council regarding the merits of applying updated data for baseline health effect incidences, prevalence rates, and other population characteristics as described in chapter 6. These updated incidence/prevalence data include:

a. Updated county-level mortality rates (all-cause, non-accidental, cardiopulmonary, lung cancer, COPD) from 1994-1996 to 1996-1998 using the CDC Wonder Database;
b. Updated hospitalization rates from 1994 to 1999 and switched from national rates to regional rates using 1999 National Hospital Discharge Survey results;
c. Developed regional emergency room visit rates using results of the 2000 National Hospital Ambulatory Medical Care Survey;
d. Updated prevalence of asthma and chronic bronchitis to 1999 using results of the National Health Interview Survey (HIS), as reported by the American Lung Association (ALA), 2002;
e. Developed non-fatal heart attack incidence rates based on National Hospital Discharge Survey results;

f. Updated the national acute bronchitis incidence rate using HIS data as reported in ALA, 2002, Table 11;
g. Updated the work loss days rate using the 1996 HIS data, as reported in Adams, et al. 1999, Table 41;
h. Developed school absence rates using data from the National Center for Education Statistics and the 1996 HIS, as reported in Adams, et al., 1999, Table 46.
1. Developed baseline incidence rates for respiratory symptoms in asthmatics, based on epidemiological studies (Ostro et al. 2001; Vedal et al. 1998; Yu et al; 2000; McConnell et al., 1999; Pope et al., 1991).

Charge Question 14. EPA plans to initiate an expert elicitation process to develop a probability-based method for estimating changes in incidence of PM-related premature mortality. Plans for this expert elicitation are described in chapter 9 of this blueprint, and a separate charge question below requests advice from the Council pertaining to the merits of the design of this expert elicitation. EPA recognizes, however, the possibility that this expert elicitation process may not be fully successful and/or may not be completed in time to support the current 812 analysis. Therefore, in order to facilitate effective planning and execution of the early analytical steps which provide inputs to the concentration-response calculations, EPA seeks advice from the Council regarding the scientific merits of alternative methods for estimating the incidences of PM-related premature mortality, including advice pertaining to the most scientifically defensible choices for the following specific factors:

a. Use of cohort mortality studies, daily mortality studies, or some combination of the two types of studies
b. Selection of specific studies for estimating long-term and/or short-term mortality effects
c. Methods for addressing –either quantitatively or qualitatively– uncertain factors associated with the relevant concentration-response function(s), including
i. Shape of the PM mortality C-R function (e.g., existence of a threshold),
ii. PM causality,
iii. PM component relative toxicity, and
iv. PM mortality effect cessation lag structure
v. Cause of death and underlying health conditions for individuals dying prematurely due to chronic and/or short term exposures to particulate matter
vi. The use of ambient measures of exposure for estimating chronic health effects, given recent research reviewed in the NAS (2002) report that questions the implications of using ambient measures in cohort studies

Charge Question 15. EPA estimates of benefit from particulate control may underestimate the impact of nonfatal cardiopulmonary events on premature mortality and life expectancy. For the base analyses, which rely on cohort evidence, the limited follow-up periods for the cohorts may not fully capture the impacts of nonfatal cardiovascular events on premature mortality later in life. For the alternative analyses –including cost-effectiveness analyses– which rely more on acute studies and life-expectancy loss, the years of life are estimated only for fatal events. Yet nonfatal events such as myocardial infarction reduce a person's

life expectancy by a substantial percentage.

a. Do you agree that EPA, in the 812 analyses, should adjust benefit estimates to account for the mortality effects of non-fatal cardiovascular and respiratory events?

b. What medical studies and mathematical models of disease might be useful to review or use if EPA moves in this direction?

c. When the nonfatal events are valued in economic terms, should EPA assume that the published unit values for morbidity already account for the life-expectancy loss or should an explicit effort be made to monetize the resulting longevity losses?

Charge Question 16. In recent EPA rulemakings, EPA's "base estimate" of benefit from PM control has been based on cohort epidemiological studies that characterize the chronic effects of pollution exposure on premature death as well as capturing a fraction of acute premature mortality effects. If these chronic effects occur only after repeated, long-term exposures, there could be a substantial latency period and associated cessation lag. As such, a proper benefits analysis must consider any time delay between reductions in exposure and reductions in mortality rates. For the acute effects, such as those considered in EPA's alternative benefit analyses, the delays between elevated exposure and death are short (less than two months), and thus time-preference adjustments are not necessary.

a. In the previous 812 analysis and in recent rulemakings, EPA assumed a weighted 5-year time course of benefits in which 25% of the PM-related mortality benefits were assumed to occur in the first and second year, and 16.7% were assumed to occur in each of the remaining 3 years. Although this procedure was endorsed by SAB, the recent NAS report (2002) found "little justification" for a 5-year time course and recommended that a range of assumptions be made with associated probabilities for their plausibility. Do you agree with the NAS report that EPA should no longer use the deterministic, 5-year time course?

b. One alternative EPA is considering is to use a range of lag structures from 0 to 20-30 years, with the latter mentioned by NAS in reference to the Nyberg et al PM lung cancer study, with 10 or 15 years selected as the mid-point value until more definitive information becomes available. If this simple approach is used, should it be applied to the entire mortality association characterized in the cohort studies, or only to the difference between the larger mortality effect characterized in the cohort studies and the somewhat smaller effect found in the time series studies of acute exposure? Should judgmental probabilities be applied to different lags, as suggested by NAS?

c. Another option under consideration is to construct a 3-parameter Weibull probability distribution for the population mean duration of the PM mortality cessation lag. The Weibull distribution is commonly used to represent probabilities based on expert judgment, with the 3-parameter version allowing the shaping of the probability density function to match expected low, most likely, and expected high values. EPA is still considering appropriate values for the low, most likely, and expected high values –and therefore for the Weibull shape and location parameters– and EPA is interested in any advice the Council wishes to provide pertaining to the merits of this approach and/or reasonable values for the

probability distribution.

Charge Question 17. In support of Clear Skies and several recent rule makings the Agency has presented an Alternative Estimate of benefits as well as the Base Estimate. EPA developed the Alternative Estimate as an interim approach until the Agency completes a formal probabilistic analysis of benefits. NAS (2002) reinforced the need for a probabilistic analysis. The Alternative Estimate is not intended as a substitute method and needs to be considered in conjunction with the Base Estimate. Presentation of Base and Alternative estimates in the 812 Report may not be necessary if the probability analysis planned for the 812 Report is successful. While the Base Estimate assumes that acute and chronic mortality effects are causally related to pollution exposure, the Alternative Estimate assumes only acute effects occur or that any chronic effects are smaller in size than assumed in the Base Estimate. The Council's advice is sought on the following matters:

a. It has been noted by some particle scientists that the size of estimates based on time series studies that incorporate a distributed lag model, accounting for effects of 30 to 60 days after elevated exposure, may be similar in size to some interpretations of the results from the cohort studies. Does the Council agree that it is a reasonable alternative to use an estimate of the concentration-response function consistent with this view? If the Council agrees with the assumption, can it suggest an improved approach for use in an Alternative Estimate? The agency also seeks advice on appropriate bounds for a sensitivity analysis of the mortality estimate to be used in support of the Alternative Estimate.

b. An assumption that a specific proportion of the PM-related premature mortality incidences are incurred by people with pre-existing Chronic Obstructive Pulmonary Disease (COPD) and that these incidences are associated with a loss of six months of life, regardless of age at death. If these values are not valid, what values would be more appropriate? Do you recommend a sensitivity analysis of 1 to 14 years (with the latter based on standard life tables), as included in the draft regulatory impact analysis of the proposed Nonroad diesel rule?

c. An assumption that the non-COPD incidences of PM-related premature mortality are associated with a loss of five years of life, regardless of age at death. If these values are not valid, what values would be more appropriate? Do you recommend a sensitivity analysis of 1 to 14 years (with the latter based on standard life tables), as included in the draft regulatory impact analysis of the proposed Nonroad diesel rule?

d. Additional quantified and/or monetized effects are those presented as sensitivity analyses to the primary estimates or in addition to the primary estimates, but not included in the primary estimate of total monetized benefits. While no causal mechanism has been identified for chronic asthma and ozone exposure, there is suggestive epidemiological evidence.

   i. Two studies suggest a statistical association between ozone and new onset asthma for two specific groups: children who spend a lot of time exercising outdoors and non-smoking men. We seek SAB comment on our approach to quantifying new onset asthma in the sensitivity analyses.

   ii. Premature mortality associated with ozone is not currently separately

included in the primary analysis because the epidemiological evidence is not consistent. We seek SAB comment on our approach to quantifying ozone mortality in the sensitivity analyses.

iii. Does the Council agree that there is enough data to support a separate set of health impacts assessment for asthmatics? If so, does the approach proposed by the Agency address the uncertainty in the literature?

Charge Question 29. Does the Council support the plans described in chapter 9 for the expert elicitation pilot project to develop a probability-based PM2.5 C-R function for premature mortality, including in particular the elicitation process design? If the Council does not support the expert elicitation pilot project, or any particular aspect of its design, are there alternative approaches the Council recommends for estimating PM-related mortality benefits for this analysis, including in particular a probabilistic distribution for the C-R function to reflect uncertainty in the overall C-R function and/or its components?

Charge Question 30. EPA plans to develop estimates of an independent mortality effect associated with ozone, as described in chapter 9. Does the Council support the use of the most recent literature on the relationship between short-term ozone exposure and daily death rates, specifically that portion of the literature describing models which control for potential confounding by PM2.5? Does the Council agree with the use of that literature as the basis for deriving quantified estimates of an independent mortality impact associated with ozone, especially in scenarios where short-term PM2.5 mortality estimates are used as the basis for quantifying PM mortality related benefits? Does the Council support the plans described in chapter 9 for the pilot project to use this literature to develop estimates of the ozone related premature mortality C-R function using the three alternative meta-analytic approaches? If the Council does not support this pilot project, or any particular aspect of its design, are there alternative approaches to quantifying ozone-related premature mortality which the Council recommends?

Charge Question 32. Does the Council support the plans described in chapter 10 for evaluating the quality of data inputs and analytical outputs associated with this study, including the planned publication of intermediate data products and comparison of intermediate and final results with other data or estimates? If the Council does not support these plans, are there alternative approaches, intermediate data products, data or model comparisons, or other data quality criteria the Council reommends? Please consider EPA's Information Quality Guidelines in this regard.

Charge Question 33. Does the Council support the plans described in Chapter 11 for the aggregation and presentation of analytical results from this study? If the Council does not support these plans, are there alternative approaches, aggregation methods, results presentation techniques, or other tools the Council recommends?

Charge Question 34. Does the Council support the plans describe in Appendix D for updating the estimated costs and benefits of Title VI programs? If the Council does not support these plans, are there alternative data, models, or methods the Council recommends?

Charge Question 35. Does the Council support the plans described in Appendix E for the benzene case study, including the planned specific data, models, and methods, and the ways in which these elements have been integrated? If the Council does not support these plans, are there alternative data, models, or methods the Council recommends?

Charge Question 36. A cessation lag for benzene-induced leukemia is difficult to estimate and model precisely due to data limitations, and EPA plans to incorporate a five-year cessation lag as an approximation based on available data on the latency period of leukemia and on the exposure lags used in risk models for the Pliofilm cohort (Crump, 1994 and Silver et al., 2002). Does the SAB support adoption of this assumed cessation lag? If the Council does not support the assumed five-year cessation lag, are there alternative lag structures or approaches the Council recommends?

# APPENDIX B
# BIOSKETCHES OF HES MEMBERS

**Mr. Fintan Hurley**

Mr. Fintan Hurley is currently Research Director at the Institute of Occupational Medicine (IOM) – an independent non-profit organization carrying out research and consulting in occupational and environmental health, exposure and risk assessment – in Edinburgh, Scotland, UK. Dr. Hurley graduated 1st Honours B.A. in Mathematics, Statistics and Economics at the National University of Ireland (NUI) in Cork in 1970; MA (NUI) Mathematics and Statistics in 1971; post-graduate research in Bayesian methods at University of Edinburgh. His main research activities have been (i) epidemiological studies of the health effects of long-term occupational exposures to dusts, pesticides and (ii) since the early 1990s, on estimating the public health impacts and associated costs of outdoor air pollution, overall and from particular sources (electricity generation and transport…). His research experience has been multi-disciplinary, working closely with physicians, toxicologist, exposure specialists, ergonomists, economists, psychologists, mathematical modelers as well as other statisticians. Since 1996 he has been a member of the Committee on the Medical Effects of Air Pollutants (COMEAP) of the UK Department of Health and was from 1998-2002 a member of the Expert Panel on Air Quality Standards (EPAQS) of the UK Department of Environment (then, DEFRA). y

**Dr. Patrick Kinney**

Dr. Kinney is Associate Professor of Clinical Public Health in Environmental Health Sciences, Sc.D. Environmental Health Sciences/Air Pollution Control and Physiology at the Harvard University School of Public Health. His areas of research include Air pollution epidemiology, exposure assessment, exposure modeling, risk assessment. He is the Author of EPA ozone and PM criteria documents - epidemiologysections ; member of NAS panel on Health Benefits Analysis.

**Dr. Michael Kleinman**

Dr.Michael T. Kleinman is a Professor of Community and Environmental Medicine at the University of California, Irvine. He has a Ph.D. in Environmental Health Sciences from New York University and a M.S. in Chemistry (Biochemical Toxicology) from the Polytechnic Institute of Brooklyn. He also holds a B.S. in Chemistry from Brooklyn College, City University of New York. Dr. Kleinman has extensive experience in studies of the effects of airborne contaminants on health. His current research activities include inhalation studies with laboratory animals and human volunteers to test hypotheses related to defining causal relationships between health effects and components of ultrafine, fine and coarse pollutant particles. A key component in these studies, which include both laboratory based and epidemiological panel research programs, is the assessment of exposure and the relationship of exposure to dose. Dr. Kleinman also has had extensive experience in determinations of atmospheric transport of chemical contaminants. Dr. Kleinman has previously served as a consultant to the HEES. He currently is a member of the executive committee of the Southern California Particle Center and Supersite which is a multi-institutional consortium based at UCLA and which is supported by USEPA and the California Air Resources Board. He is currently the Chair of the Air Quality Advisory Committee for the state of California. This committee reviews the scientific basis of air quality

regulations promulgated by the California EPA. Dr. Kleinman is a member of a National Academy of Sciences Committee to evaluate the preparation of the US Navy to operate in Chemical, Biological and Radiological Warfare situations. He was also the co-Chair of a National Academy of Sciences Committee to evaluate current capabilities related to Protection of Deployed Forces Against Chemical and Biological Weapons. He is the past chair of the Environmental Division of the Air and Waste Management Association and is a member of the executive committee of the University of California Toxic Substance Teaching and Research Program.

**Dr. Nino Künzl**i

Dr. Nino Künzli, MD PhD, former Assistant Professor (P.D.) at the Institute for Social and Preventive Medicine (ISPM) at the University of Basel (Switzerland), is Associate Professor at University of Southern California Keck School of Medicine (Department of Preventive Medicine; Environmental Health Science Division), Los Angeles. As an environmental epidemiologist, his main areas of focus are exposure to and health effects of ambient air pollution and the public health impact of these effects. He is a co-investigator and member of research teams such as the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA; Swiss National Science Foundation), the European Community Respiratory Health Survey II (European Community Research Programs), where he leads the Air Pollution Central Unit, the European Population Exposure Distribution Assessment Study (EXPOLIS), and the UC Berkeley Ozone Study (Prof. Ira Tager; NIH grant). At USC he collaborates with the repeated cohort Children Health Study on air pollution and health in 12 South Coast Basin communities (NIH). He serves on national and international expert committees and as reviewers of the major journals in this field. With the Trinational European Air Pollution Impact Assessment project, published in Lancet, he intensified particularly a debate about the interpretation of air pollution epidemiology and its application to risk assessment. The concepts published in the American Journal of Epidemiology have been subject of several committees such as from WHO, leading to methodological guidelines and further work by many others. He was a member of the U.S. National Academy of Sciences NRC Committee on Estimating the Health-Risk-Reduction Benefits of Proposed Air Pollution Regulations which also addressed the issue of how to interpret effect estimates from different study designs.

**Dr. Morton Lippmann**

Current professional affiliations and positions held by Dr. Lippman include: Professor, NYU School of Medicine,  Area(s) of expertise, and research activities and interests: Human environmental exposure assessment and associated health effects, respiratory tract dosimetry, aerosol science and technology, risk assessment .Leadership positions in national associations or professional publications or other significant distinctions: Past Chair of: EPA SAB CASAC SAB Exposure Comm. NIOSH Board of Scientific Counsellors Amer. Conf. of Governmental Industrial Hygienists, Past President: International Society of Exposure Analysis, Educational background, especially advanced degrees, including when and from which institutions these were granted: B.Ch..E. (1954) - The Cooper Union S.M. (1955) - Harvard Univ.Ph.D. (1967) - New York Univ.

**Dr. Bart Ostro**

Bart Ostro, Ph.D., is currently the Chief of the Air Pollution Epidemiology Unit, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. His primarily responsibilities are to formulate the Agency's recommendations for state ambient air quality standards and to investigate the potential health effects of criteria air pollutants. His previous research on mortality and morbidity effects of air pollution, has contributed to the determination of federal and state air pollution standards for ozone and particulate matter. Dr. Ostro was also a co-author of the EPA regulatory impact analysis that was a basis for the federal ban of lead in gasoline. Dr. Ostro has served as a consultant with several federal and international institutions including the World Health Organization and the World Bank, and with several foreign governments including Mexico, Indonesia, Italy, the European Union, Thailand, and Chile. He currently serves on the National Academy of Sciences' Committee on Estimating the Health Risk Reduction Benefits of Proposed Air Pollution Regulations, and is on the Scientific Oversight Committee for ATHENA (Air Pollution Health Effects in Europe and North America) for the Health Effects Institute. Dr. Ostro received a Ph.D. in Economics from Brown University and a Certification in Environmental Epidemiology from the State of California. He has published over 60 articles on air pollution epidemiology and environmental economics in peer reviewed journals. His current research interests involve conducting epidemologic studies on the mortality and morbidity effects of criteria air pollutants, examining the health effects of traffic, and quantifying the health benefits and associated uncertainties related to air pollution control.

**Dr. Rebecca Parkin**

Dr. Rebecca T. Parkin is an Associate Professor in the Department of Environmental and Occupational Health with a joint appointment in the Department of Epidemiology and Biostatistics in the School of Public Health and Health Services at The George Washington University. She is also the Scientific Director of the Center for Risk Science and Public Health at the University. Previously Dr. Parkin was director of Scientific, Professional and Section Affairs at the American Public Health Association; the assistant commissioner of the Division of Occupational and Environmental Health at the New Jersey Department of Health; and an environmental epidemiologist at the Centers for Disease Control. Her areas of expertise include environmental epidemiology, public health policy, vaccine risk/benefit communication, and environmental health risk assessment and communication. She has been a member of the National Research Council's (NRC's) Water Science and Technology Board; and has served on numerous committees of the NRC, the Institute of Medicine, Environmental Protection Agency, Health and Human Services, and Agency for Toxic Substances and Disease Registry. Throughout her career, she has served as a site visitor for the Council on Education for Public Health, and as a peer reviewer for several professional journals focused on environmental health. Recently, she has coauthored a book on the CCL microbial pathogens and related risk assessment issues. Dr. Parkin received her A.B. in sociology from Cornell University; M.P.H. in environmental health and Ph.D. in epidemiology from Yale University; and Certificate in Science, Technology, and Policy from Princeton University. She has been honored by Yale University as a Distinguished Alumna for her extensive public service.