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OFFICE OF THE ADMINISTRATOR  
SCIENCE ADVISORY BOARD

June 16, 2010

EPA-COUNCIL-10-001

The Honorable Lisa P. Jackson  
Administrator  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, N.W.  
Washington, D.C. 20460

Subject: Review of EPA's DRAFT Health Benefits of the Second Section 812  
Prospective Study of the Clean Air Act

Dear Administrator Jackson:

In response to a request from EPA's Office of Air and Radiation (OAR), the Advisory Council on Clean Air Compliance Analysis (Council) convened the Health Effects Subcommittee (HES) with additional experts from the Council to review EPA's draft benefits and uncertainty documents supporting the second prospective study of the benefits and costs of the Clean Air Act. The study was conducted in concordance with Section 812 of the Clean Air Act Amendments of 1990. Specifically, the HES provided advice on the data chosen for the analysis, the selection of models used to conduct the analysis, and the validity of resulting estimates of Clean Air Act program benefits.

The HES compliments EPA on a thorough analysis of a very complex issue. The Second Prospective Study has been under development for several years. In the early planning phases, the analytical blueprint and preliminary data were reviewed by the Council and its subcomponents. EPA has thoughtfully and thoroughly considered previous advice in conducting this analysis.

The HES finds the data sources and analytical methodology for estimating health benefits to be generally sound and well conceived. In particular, the HES notes that reductions in particulate matter (PM)-related mortality that can be attributed to the Clean Air Act are a major driver of benefits. The benefit estimates that EPA derives for PM are based on two well-researched and highly respected cohort studies of air pollution health effects, the Harvard Six Cities Study and the American Cancer Study (ACS) Cancer Prevention Study. These are good foundations for the health benefits estimates for PM and these studies are supported by other recent studies and expert evidence gathered by the EPA project team. This is encouraging, and the HES makes some recommendations on how to express a best estimate and the uncertainty

around that estimate. The HES generally agrees with other decisions made by the EPA project team with respect to PM, in particular, the PM mortality effect threshold model, the cessation lag model, the inclusion of infant mortality estimation, and differential toxicity of PM.

The HES supports the inclusion of mortality related to ozone exposure in the Section 812 Prospective Analysis and supports EPA's data choices for estimating health benefits from reduction in ozone exposure. As with PM, the HES makes recommendations on a statistical approach to better capture the best estimate and uncertainty around the ozone concentration-response function.

The HES finds that the draft documents presented to it for review require a fair amount of technical editing to make the analyses clearer. The details of the conclusions and recommendations are detailed in the Subcommittee's report. We appreciate the opportunity to provide EPA advice on its analysis of the health benefits of the Clean Air Act regulations.

Sincerely,

*/Signed/*

Dr. James K. Hammitt, Chair  
Advisory Council on Clean Air  
Compliance Analysis

*/Signed/*

Dr. John Bailar, Chair  
Health Effects Subcommittee

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# 1. EXECUTIVE SUMMARY

The Clean Air Act Amendments of 1990 included specific language in Section 812 directing the EPA to perform benefit-cost studies of the overall effects of the Clean Air Act. In response to Section 812, on October 15, 1997, EPA issued a retrospective study (1970 – 1990) of benefits and costs of the Clean Air Act. EPA issued a first prospective study (1990 – 2010) on November 15, 1999 and is now completing a second prospective study (1990 – 2020).

The Health Effects Subcommittee (HES) of the Advisory Council on Clean Air Compliance Analysis (Council) held a public meeting on December 15-16, 2009 to review and provide guidance to the EPA on the draft human health effect estimates in chapters from the second Section 812 Prospective Analysis benefits report (1990 – 2020) as well as the human health components of the draft stand-alone uncertainty analysis report. Specifically, the OAR asked the HES to consider: (1) the data choices and methodologies used to develop mortality estimates as a function of air pollution concentration for both particulate matter (PM) and ozone; (2) The methods and data used to develop estimates of the lag time between cessation of exposure and reduction in health effects for both PM and ozone; (3) the Agency's assumptions about a threshold concentration for mortality effects for both PM and ozone; (4) the estimates of infant mortality related to PM exposure; (5) Baseline incidence and prevalence of relevant disease conditions in the population; (6) the sensitivity analysis of the analytical results to differences in PM composition; and (7) the approach for dynamic modeling of U.S. population demographic changes.

Overall, the HES finds the EPA analyses, data choices, and methodologies to be sound. EPA bases its estimates of the mortality benefits of reducing fine particulate matter (PM<sub>2.5</sub>) on data analyzed from two large, long-running landmark studies on the health effects of air pollution, the Harvard Six Cities Study and the American Cancer Society (ACS) Cancer Prevention Study (CPS). The HES finds the selection of these cohort studies as the underlying basis for PM mortality benefit estimates to be a good choice. These are widely cited, well studied and extensively reviewed data sets. EPA further bolsters its PM mortality benefit estimates by gathering information on the PM mortality concentration-response function in an expert elicitation of twelve clinicians, epidemiologists, and air pollution scientists. HES suggests an alternative to EPA's choice of the Pope et al. (2002) study (based on the ACS cohort) for the primary estimates of differences in incidence of PM-related premature mortality and the Laden et al. (2006) study (based on the Six Cities cohort) as an alternative estimate. EPA found that these choices fell at approximately the 25<sup>th</sup> and 75<sup>th</sup> percentile of the mortality effect estimates garnered from the expert elicitation. EPA proposed a statistical approach using copula functions to combine the 12 expert elicitation estimates into a single mortality effects distribution. The HES, however, recommends a simpler approach. EPA should define a distribution, perhaps a truncated normal distribution, with the Pope and Laden studies at the 25<sup>th</sup> and 75<sup>th</sup> percentiles respectively. The mean of the new distribution should then be close to the mean of the central estimates of both Pope and Laden. This generally will be consistent with the distribution identified in the expert elicitation.



The HES agrees with EPA's contention that a majority of health effect benefits from reduction of exposure to PM occurs within the first few years following reduced exposure. The HES therefore supports EPA's choice of a 20-year distributed cessation lag structure, skewed towards benefit gains in the first few years. However, EPA should further examine the decay function and determine whether a more rapid decay model is appropriate. Further, the HES fully supports EPA's use of a no-threshold model to estimate the mortality reductions associated with reduced PM exposure.

EPA estimates an association between PM exposure and respiratory inflammation and infection leading to mortality in children under 5 years of age, relying on a cohort study (Woodruff et al., 1997). The HES generally supports this approach with some caveats. The age range of interest for respiratory-related mortality should be 1 month of age (since infections earlier than this are not likely to be from air pollution) to about 12 months of age. There are limited data available to estimate these effects and EPA should better describe the data challenges and uncertainties in these estimates.

The HES supports the inclusion of mortality due to ozone exposure in the Section 812 Prospective Analysis, given the evidence in the time-series literature and the consistency of these findings with morbidity studies. With respect to the concentration-response estimates, it is premature to use the cohort mortality evidence from Jerrett et al., 2009 as the basis for the Primary Estimate, because it has not yet been subjected to the vigorous critique that now supports, for example, analyses using the Pope and Laden studies for PM. For the time-series ozone mortality evidence, the HES supports the consideration of both the multi-city studies and the literature meta-analyses when generating the Primary Estimate. As there is not a clear basis for choosing one set of studies over the other, the HES recommends that the Primary Estimate be derived as an intermediate value between the multi-city studies and the meta-analyses. The uncertainty distribution can then reflect methodological uncertainties as well as the uncertainties reported within individual studies.

The HES supports the EPA decision not to apply a cessation lag for ozone and also supports the assumption of no threshold for ozone-related mortality effects, as evidence is not conclusive to demonstrate such a threshold.

In their analysis, EPA incorporates data on the baseline incidence and prevalence of the various health endpoints that are the basis of the benefits. The HES generally supports the choices made by the EPA. The most important data, in terms of driving the benefit estimates, are the baseline mortality data, which are of relatively high quality. There is some concern about the noise and inconsistency in data used to estimate baseline school loss and work loss days. There may be too much noise to make reasonably reliable quantitative estimates of air pollution work loss days.

The Council had previously recommended that EPA perform an analysis of the sensitivity of their benefit results to differing PM composition in terms of both size and chemical composition. EPA determined that there are insufficient data to perform such an analysis. The HES supports this conclusion, given the state of the evidence but encourages EPA to continually revisit this conclusion as the literature evolves.

EPA developed a dynamic population simulation model to explore how changes in population age structure change pollution-related premature mortality risks. EPA asked HES to comment on the methodology and results and to consider providing advice on the potential utility of further development of this approach. Overall, the HES commends EPA for demonstrating how dynamic population modeling can be used in estimating the mortality impacts of long-term exposure to PM<sub>2.5</sub>. If practical, the approach would be a preferred one. However, the HES recognizes that these methods are complicated and computationally intensive, necessitating trade-offs between resolution of the results and run-time for the models. The HES recommends that the EPA describe in more detail the methods used and the reasons why EPA chose these particular methods over others.

Overall, the HES finds the EPA analysis thorough and generally consistent with previous recommendations from the Council. The HES makes some minor suggestions for improvement and notes that the draft documents presented to the HES need technical editing to make the analyses and associated uncertainties more clear.

## 2. BACKGROUND

The reauthorization and amendment of the Clean Air Act in 1990 included specific language in Section 812 directing the EPA to perform benefit-cost studies of the programs affiliated with the Clean Air Act as a whole, relative to a consistent baseline. Congress expressed their intent that the comprehensiveness of the 812 studies should encourage and enable EPA to develop and continually refine its capabilities in clean air program assessment. Congress' stated objective was to ensure that EPA could provide better information on clean air program benefits and costs in support of future rounds of Clean Air Act reauthorization, whenever they may occur.

Included in the Section 812 amendments was specific language requiring EPA to convene a panel of outside experts in a range of relevant disciplines to advise the Administrator on the data chosen for the analysis, the selection of models used to conduct the analysis, and the validity of resulting estimates of Clean Air Act program benefits and costs. The Advisory Council on Clean Air Act Compliance Analysis (Council) was established in 1991 to fulfill this goal of providing multi-disciplinary outside expert review. Separate subcommittees have since been established to advise the parent Council on particular technical aspects of the Section 812 studies. The Air Quality Modeling Subcommittee (AQMS) was formed to advise the Council on issues of emissions estimation and air quality modeling. A Health Effects Subcommittee (HES) and an Ecological Effects Subcommittee (EES) exist today to advise the Council on issues associated with human health effects and ecological effects components, respectively.

In response to the Section 812 legislation, on October 15, 1997, EPA issued a retrospective study (1970 – 1990) of the benefits and costs of the Clean Air Act. EPA issued a first prospective study (1990 – 2010) on November 15, 1999 and is now completing a second prospective study (1990 – 2020).

In the Charge to the Committee, EPA requested that the HES review the human health-related chapters and appendices of the draft Section 812 Second Prospective Study benefits and uncertainty reports, and respond to the following general questions:

- a. Does the Council HES support the data choices made by the 812 Project Team for the development of the human health-related chapters and appendices of the draft benefits and uncertainty reports? If not, are there alternative data sets the Council HES recommends should be applied instead?
- b. Does the Council HES support the methodological choices made for analyzing those data and developing the human health effect estimates for the relevant scenarios, and for characterizing their uncertainty? If not, are there alternative methodologies the Council HES recommends should be applied instead?
- c. What advice does the HES have for the Council regarding the validity and utility of the human health effect analyses incorporated in the draft benefits report and the uncertainty

analyses incorporated in the draft uncertainty report? If the validity and/or utility of the reports and their underlying analyses could be improved, what specific improvements does the Council HES recommend that the 812 Project Team consider, either for the present analysis or as part of a longer term research and development program?

Additional detailed questions also were posed that pertain to specific subsections of the review materials.

The purpose of this Advisory is to review and provide guidance on the EPA draft human health effect estimates in chapters from the Second Section 812 Prospective analysis benefits report (1990 – 2020) as well as the human health components of the draft stand-alone uncertainty analysis report.

The Health Effects Subcommittee (HES) held a public meeting on December 15-16, 2009 to receive briefings and discuss the charge questions provided by the Agency. In addition to the Chair of the HES, who represents the HES on the Council, several members of the Council participated in the meeting, including Dr. James Hammitt, Chair of the Council, Dr. Michelle Bell, Dr. Jonathan Levy, and Dr. Arden Pope. A subsequent conference call of this committee was held on March 2, 2010, for the purposes of discussing recommendations made in this report. The HES report was discussed and approved by the full Council at the public meeting on May 4, 2010.

### 3. GENERAL COMMENTS

The Council HES found the draft report to be generally sound, and members commend EPA on the quality of the present version. The very quality of this draft has made detailed criticism more feasible. EPA had to make an enormous number of choices of data collected from a variety of sources, and, using a variety of models, further processed the data. The scope and complexity of the data cannot be fully documented in a report of manageable size. Insofar as we have been able to probe the data, the Council HES generally supports the data approaches and judgments that have been made.

In particular, the HES supports the presentation of the PM mortality effect estimates and the data choices using the Pope et al. (2002) and Laden et al. (2006) studies. The HES notes that using the Pope studies (which are based on the ACS studies) for the Primary Estimate would provide lower health benefits estimates than the Six Cities study, which is considered by EPA to be equally applicable for health benefits analysis. The HES supports EPA's aim to give unbiased benefits estimates where possible. The HES proposes an alternative simple combination of the Pope and Laden studies. This alternative is discussed in the HES response to charge question 2a on the PM mortality concentration response function. With respect to PM, the HES also generally supports the Agency's proposed 20-year distributed cessation lag model, though most of the benefits of cessation appear to occur in the first few years after cessation of exposure. The HES commends the efforts to quantify infant mortality related to PM, even though, as the EPA acknowledges, these do not add a large amount to the overall benefits in the 812 Analysis, and the estimates are based on only a small number of studies. The HES also supports the Agency's choice of a no-threshold model for PM-related effects.

The generation of a concentration-response function to estimate mortality effects of ozone is more difficult. The HES supports EPA's data choices for the Primary Estimates. Because time series studies were used for the Primary Estimate, a cessation lag for effects is not relevant, and the HES supports the Agency's use of a no-lag assumption for the primary mortality effect estimates for ozone. Finally, the HES supports EPA's use of a no-threshold model for ozone mortality effects, based on the time-series results. The HES supports the inclusion of, as an alternate estimate of benefits, a concentration-response function (CRF) from long-term exposure based on Jerrett et al. (2009).

There should be a short but thoughtful discussion of the purposes of the benefits report and how it may be used beyond the initial determination of the overall impact of the Clean Air Act and its amendments. There should also be some consideration of the likely background of expected readers (Congressional staffers? State health officials? Other?), and the report should be written to be comprehensible to them. This includes spelling out the meaning of, and assumptions underlying concepts such as Value of Statistical Life (VSL), which appear easy to understand but which have quite precise and non-intuitive technical meanings. Overall the report needs technical editing, and two sections (Chapter 6, PM mortality cessation lag and Chapter 7, Dynamic population modeling) are difficult to follow; these sections may need a complete re-write to achieve better clarity for non-experts.

The HES makes some general observations and recommendations for improvement of the presentation in the draft documents. EPA generally models health effects in ways that imply multiplicative effects. The report should discuss this and say why other models (e.g., additive) were not used. The report should also explicitly say why it is limited to PM and ozone, when EPA regulates a much larger number of pollutants.

There is no discussion of the differences between values at central monitors and what people actually inhale. The HES recognizes that broad data on inhaled levels of pollutants do not now exist, but some comment is in order. (Elementary considerations of epidemiology suggest that better measures of what is inhaled would probably lead to bigger estimates of effects).

The characterization of uncertainty is confusing and incomplete. It would be helpful to have an integrated assessment of overall uncertainty. Are the estimates within 10% of the true value? 50%? 200%? Does it matter? Missing is a sense of what level of accuracy is needed in this report and how close the report may come to that. It is understandable that this is difficult to say, so uncertainty is broken down into components. However, the appendices are not comprehensive and the scope for “comprehensiveness” is not stated. It is not clear how the authors determined “key uncertainties”. Rather than brief footnoted statements, it would be helpful to have introductory text describing the scope of the uncertainties listed, the significance classification definitions (e.g., “potentially major” and “probably minor”), and rationales for these choices. Further, it would be helpful to know the likely direction of bias and EPA’s confidence in the assessment components.

On a related note, there are inconsistencies in presenting assumptions between the Benefits and Uncertainty draft reports. A comparison of the assumptions (using a simple search on the “assum” in both documents) reveals a mismatch that may not be a problem but is a matter for clarification. Two sets of authors may have used different approaches or boundaries for identifying and/or recording assumptions. Perhaps the authors of the benefits document sought to present all assumptions they made in their estimation processes; e.g., in extending study-specific or regional results to the national scale. If so, the rationale for some assumptions is not always clear (e.g., use of mother’s median wage rather than an average of mother and father median wages, which may yield a higher cost estimate). In contrast, the authors of the uncertainty report indicate that they intended to record only the most important assumptions made during their estimation processes.

The HES suggests that a section be added to the report that compiles, in a brief form, the primary and secondary data sources and the model sources used. This section should include links to detailed descriptions of the data and models used. Finally, the report reveals a large number of research needs. It would help readers to add some discussion of the most important gaps, especially if EPA is to repeat this exercise at some future time.

Overall, total mortality benefits from the Clean Air Act appear large in relation to total US mortality (about 7%). The report should note that this result is driven in part by the rise in expected pollution-related mortality in the absence of Clean Air Act, and not entirely by actual

reductions in mortality. If EPA can estimate these separately, the report will be stronger and perhaps more credible.

## 4. RESPONSE TO SPECIFIC CHARGE QUESTIONS

### 4.1. PM Mortality Concentration-Response Function (CRF)

Agency-supplied background: The current draft benefits report reflects adoption of the Pope et al. 2002 study as the basis for the Primary Estimates of the difference in incidences of PM-related premature mortality. Also within the main benefits report, an Alternative Estimate is presented prominently which is based on the Laden et al. 2006 study. Furthermore, the Project Team is currently assessing the potential significance of the recent Krewski et al. (2009) publication since it appears to strengthen the evidence for PM-related ischemic heart disease and lung cancer mortality and could provide the basis for a revised Primary Estimate or an additional Alternative Estimate. Uncertainty in the Primary Estimate is further described in the draft uncertainty report through graphical presentation of results obtained by applying each of the 12 expert elicitation study functions to the differences in PM exposure estimated for the with-CAAA90 and without-CAAA90 core scenarios. In addition, the Project Team has recently been considering an approach developed by Industrial Economics, which uses a copula function to generate results representing the 12 expert functions. This approach is summarized in a draft briefing which the Project Team proposes to present to the HES on December 15 for its consideration.

Charge question 2a: Does the Council HES support these study selections and the organization and presentation of PM mortality estimates in the draft benefits and uncertainty reports? In addition, a particular question for which the Project Team seeks HES advice is whether the application of mortality risk coefficients drawn from the Krewski et al. (2009) study should be considered for use in generating the Primary Estimate, or at least as the foundation for an Alternative Estimate. If the answer to either or both of these two questions is negative, are there alternative study choices and/or methods for generating, organizing, and presenting results which the Council HES recommends EPA consider?

HES response: The HES emphasizes the continued importance of the American Cancer Society (ACS) and Harvard Six Cities cohort studies for underpinning our understanding of the mortality effects of PM<sub>2.5</sub> in the U.S. Findings from both cohorts have been robust to extensive analyses and independent re-analyses. The HES believes that the Pope et al. (2002) and Laden et al. (2006) analyses of the ACS and Six Cities cohorts, respectively, are at present the most useful findings from these studies. The Krewski et al. (2009) findings, while informative, have not yet undergone the same degree of peer review as have the aforementioned studies. Thus, the HES recommends that EPA not use the Krewski et al. (2009) findings for generating the Primary Estimate.

The HES also reviewed the findings from EPA's Expert Elicitation (EE) study. The central effect estimates from the 12 experts cover a range that encompasses the Pope et al. (2002) effect estimate at the low end, and the Laden et al. (2006) effect estimate at the high end. This is illustrated in Figure 1 (reproduced from an EPA Technical Memorandum presented to the HES), which shows the monetized PM-related mortality benefits associated with meeting a hypothetical 50 ppb NO<sub>2</sub> standard in 2020 for the studies of Pope et al. and Laden et al. as well as

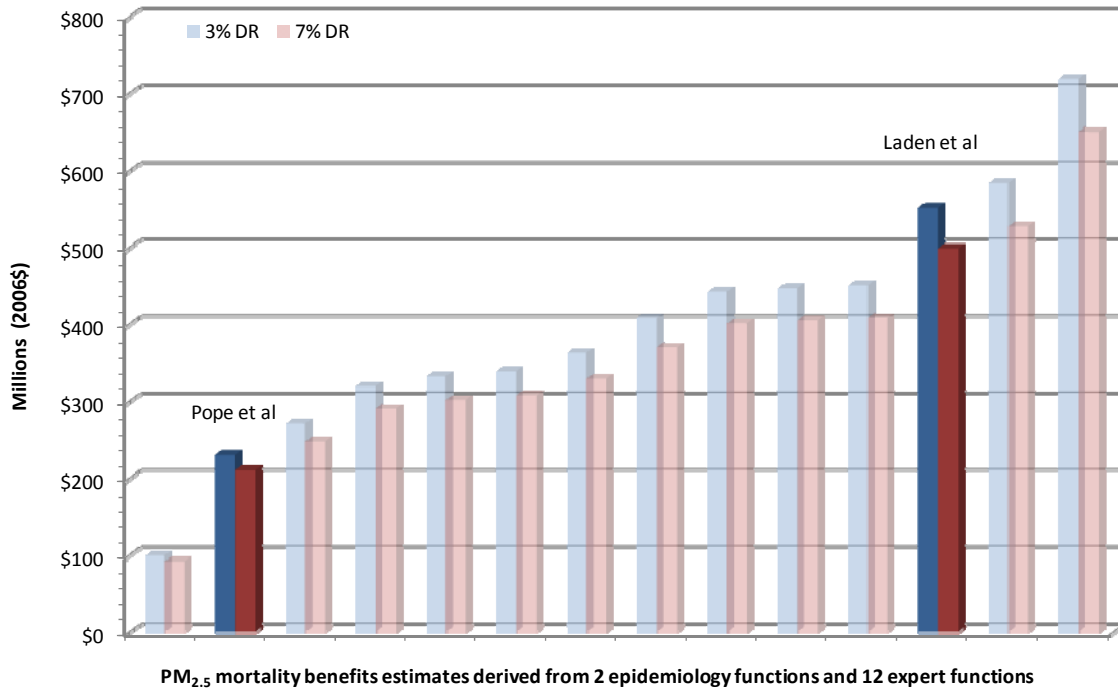


the twelve experts consulted in the EE study. Further, a quantitative analysis by EPA consultants demonstrates that the Pope et al. (2002) effect estimate falls at about the 25<sup>th</sup> percentile of the EE distribution; the Laden et al. (2006) effect estimate falls at about the 75<sup>th</sup> percentile of the EE distribution. HES reviewed the proposed copula function approach to combine the 12 response functions from the EE. A copula function is a useful method to describe the dependence among a set of random variables. When information about dependence is limited or absent, a joint distribution can be constructed from the marginal distributions of the variables by making assumptions about the copula function. While supporting EPA's investigation of alternatives for combining evidence using advanced quantitative methods, the HES feels that adoption of the copula function approach as a prominent feature of the current prospective analysis might hinder interpretability and transparency of the findings for a general audience, given the very technical nature of the method.

The HES finds that the EE results from 2006 remain relevant; i.e., that new evidence since 2006 informs, but does not fundamentally contradict, the earlier data. On that basis, the HES supports the EE as the most comprehensive assessment to date of the mortality effect of PM<sub>2.5</sub> and so, given EPA's stated objective of generating unbiased benefits estimates in the Section 812 prospective analysis, HES recommends that EPA adopt a new approach for developing its primary mortality benefits estimates. The new approach should reflect the range of EE opinions in a transparent way, while grounding the risk estimates in results from the two major contributing US cohorts. We suggest an approach along the following lines:

Define a distribution of possible coefficients (perhaps a truncated normal distribution with zero probability below a value of zero, or a gamma distribution), with 25<sup>th</sup> percentile equal to a 0.6 percent change in mortality per 1  $\mu\text{g}/\text{m}^3$  change in annual average PM<sub>2.5</sub> (the Pope et al., 2002 central estimate), with 75<sup>th</sup> percentile equal to 1.5 percent change in mortality per 1  $\mu\text{g}/\text{m}^3$  change in annual average PM<sub>2.5</sub> (the Laden et al., 2006 central estimate), and with mean equal to approximately the mean of these two values. Such a distribution would be adopted for the primary estimates.

The HES considered a formal method of integrating the opinions of the elicited experts, using a copula function. However, the HES decided not to recommend this approach, favoring instead a simpler and more transparent approach as described above.



**Figure 1. PM-related monetized benefits of attaining an NO<sub>2</sub> standard of 50 ppb nationwide in 2020.** Blue bars are based on a 3% discount rate; red bars represent a 7% discount rate (Source: Fann, 2009).

#### 4.2. Cessation Lag

Agency-supplied background: The Primary Estimates for PM mortality reflect an assumed lag between cessation of exposure and realization of the change in health effect incidence. Based in part on prior Council HES advice, the primary estimates in the draft benefits report reflect a 20-year distributed lag. Specifically, 30 percent of the total reduced incidences is assumed to occur in the first year following the exposure change. Another 50 percent of the total incidence changes is spread evenly over years two through five. The remaining 20 percent of the incidence change is spread evenly over years six through twenty. The effect of the cessation lag is realized through discounting (at a 5 percent rate) of the monetized value of future-year incidence changes (i.e., there is no need, and no intent, to represent the discounted values as reflecting direct discounting of incidences *per se*). In addition, the draft uncertainty report evaluates the effect of alternative lag structures. These alternatives include the 5-year distributed lag applied in the First Prospective Study and a set of smoothed lag functions derived from consideration of the results of available cohort and intervention studies.

Charge question 2b: Does the Council HES support the use of the 20-year distributed lag structure described above for generation of the Primary Estimates of the monetary value of PM mortality incidence reduction and the specific alternative lag functions presented in the draft uncertainty report? If not, are there alternative study choices and/or methods for organizing and presenting results that the Council HES recommends EPA consider?

HES response: EPA has done an admirable job responding to the suggestions of earlier reviews by the Council and NAS. However, EPA should cite and include information from the

recent analyses of the Nurses' Health Study (Puett et al., 2009) and the Harvard Six Cities Study (Schwartz et al., 2008; Laden et al., 2006). These studies suggest that most of the health effects of exposure (and benefits from reduction) occur within a few years. EPA assumes that 80% of the risk reduction occurs in the first five years. However, the EPA analysis of alternative assumptions about the lag using a given cohort study indicates that the 20-year distributed lag default assumption generates a result that is close to the mean of a range of reasonable assumptions. Therefore, in the face of uncertainty, this lag structure is appropriate.

The HES suggests that if the decay function approach is used, EPA should ensure that its choice of parameter  $k$  is consistent with its choice of risk coefficient, in terms of the cohort studies used to generate both.

### **4.3. PM-Related Infant Mortality**

Agency-supplied background: EPA's current approach to estimating the association between PM exposure and respiratory inflammation and infection leading to premature mortality in children under 5 years of age relies on the cohort study conducted by Woodruff et al. (1997). This is based in part on prior (SAB-HES) advice, which noted several strengths of the study, including the use of a larger cohort drawn from a large number of metropolitan areas and efforts to control for a variety of individual risk factors in infants (e.g., maternal educational level, maternal ethnicity, parental marital status, and maternal smoking status). A more recent study by Woodruff et al. (2006) continues to find associations between PM<sub>2.5</sub> and infant mortality, and also found the most significant relationships with respiratory-related causes of death.

Charge question 2c: Does the Council HES recommend continued reliance on the Woodruff et al. (1997) study to characterize the association between PM exposure and respiratory inflammation and infection leading to premature mortality in children under 5 years of age, or recommend that the relationship be characterized by the more recent Woodruff et al. (2006) study, or recommend some other approach that relies on a third study or some combined consideration of multiple studies? Are there specific reasons to favor the results of one of these studies or of another study?

HES response: The HES supports EPA's decision to include infant mortality in its analysis. Although its inclusion has only a small impact on overall benefits, compared with PM effects on adult mortality, incorporating infant mortality not only is consistent with the Agency's goal of comprehensiveness but also demonstrates the impacts of PM across the entire human lifespan.

An increasing body of literature relates infant mortality and PM exposure. For example, the Ritz et al., 2006 study of Southern California data further informs the PM-infant mortality relationships found in the Woodruff et al. (1997, 2006) studies. While there are some important differences between the available studies within and outside of the United States, the results consistently show positive associations between PM (both PM<sub>10</sub> and PM<sub>2.5</sub>) and infant mortality. When PM<sub>10</sub> results are scaled to estimate PM<sub>2.5</sub> impacts, the results yield similar risk estimates. The number of studies now available may be sufficient to consider pooling results, rather than relying on a single study, thereby deriving a more robust risk estimate. The strengths and

weaknesses of each study should be assessed to determine whether pooling or using a single study is the appropriate approach for this analysis.

To summarize, several studies, both within and outside of the U.S., have resulted in similar risk estimates for PM impacts on infant mortality. The committee recommends that EPA do a reasoned evaluation of relevant studies and synthesize evidence across the studies.

#### **4.4. PM Mortality Effect Threshold**

Agency-supplied background: Consistent with prior Council and NAS advice, the Project Team did not attempt to alter the Pope 2002 CRF to reflect an assumed concentration threshold below which PM concentration changes would yield no change in estimated incidences. In addition to the lack of compelling evidence for particular effects thresholds, the Project Team is not aware of any valid procedure for the altering the CRF above an assumed threshold. In other words, the Project Team presumed that imposition of an (arbitrary) threshold would require respecification of the CRF to ensure a “with threshold” CRF slope that would accurately account for the total change in incidence expected based on the epidemiological study from which the CRF was derived. Prior efforts to apply a threshold simply truncated the incidence change estimated from a no-threshold CRF, though prior SAB advice indicates this is improper and the Project Team chose not to apply such an adjustment in the current analysis.

Charge question 2d: Does the Council HES support the use of a no-threshold model for generation of the Primary Estimates of PM mortality incidence reduction? If not, are there methods for estimating and applying an effects threshold that the Council HES recommends EPA consider, either for the Primary Estimates or for presentation in the draft uncertainty report?

HES response: The HES fully supports EPA’s decision to use a no-threshold model to estimate mortality reductions. This decision is supported by the data, which are quite consistent in showing effects down to the lowest measured levels. Analyses of cohorts using data from more recent years, during which time PM concentrations have fallen, continue to report strong associations with mortality. Therefore, there is no evidence to support a truncation of the CRF.

#### **4.5. Ozone Mortality Concentration-Response Function (CRF)**

Agency-supplied background: Based in part on prior Council and NAS advice, EPA has included changes in ozone-related premature mortality as part of the Primary Estimate of benefits in the draft benefits report. Recognizing the ongoing uncertainty regarding the appropriate study or studies from which a quantitative CRF should be derived, the Project Team adopted a placeholder function for the Primary Estimate of changes in ozone mortality which encourages focus on several key factors: study selection, pooling across studies, and pooling methodology. Given the particular uncertainties regarding the reasonableness of pooling across the multi-city NMMAPS 11 studies and the meta-analyses, the Project Team specified a CRF for the Primary Estimate which reflects inverse variance-weighted pooling of the Bell et al. 2004 and Schwartz 2005 mortality effect estimates, both of which reflect an all-cause mortality endpoint. In addition, the draft uncertainty report presents alternative results obtained by applying CRFs derived from each of the three individual multi-city time-series studies and three meta-analyses. Furthermore, EPA has developed an alternative CRF based on the Jerrett et al.

(2009) long-term ozone mortality study. This approach is described in the technical memorandum included in the package of review documents.

Charge question 2e: Does the Council HES support the use of the ozone mortality CRF derived by pooling the Bell et al. (2004) and Schwartz (2005) studies for the Primary Estimate and the presentation of the six alternative estimates in the draft uncertainty report? A particular question for which the Project Team seeks HES advice is whether application of the respiratory mortality risk estimate drawn from Jerrett et al. (2009) might be suitable for use in generating the Primary Estimate, or at least for generation of an Alternative Estimate. If the answer to either, or both, of these two questions is negative, are there alternative study selection and/or pooling approaches the Council HES recommends EPA consider for the Primary Estimate in the draft main benefits report and/or for the Alternative Estimates presented in the draft uncertainty report?

HES response: The HES supports the inclusion of ozone mortality in the Section 812 Prospective Analysis, given the growth of evidence in the time-series literature and the consistency of these findings with morbidity studies. In terms of the most appropriate ozone CRF, the HES finds that it is premature to use the cohort mortality evidence from Jerrett et al. (2009) as the basis for the Primary Estimate, in light of the lack of corroboration from other cohort studies. However, the HES supports its inclusion as an Alternative Estimate or other sensitivity analysis, as it would be valuable to convey its implications if, as we expect, the cohort mortality findings are corroborated elsewhere.

For the time-series ozone mortality evidence, the HES supports the consideration of both the multi-city studies and the literature meta-analyses when generating the Primary Estimate. The multi-city studies have the advantage of a consistent methodology across cities and the possible reduction of publication bias, but meta-analytic approaches are the foundation of the CRFs elsewhere in the prospective analysis. In addition, some investigators have noted that the National Mortality, Morbidity, and Air Pollution Study (NMMAPS) produces significantly lower CRFs than other epidemiological investigations, which may be in part attributable to the question investigated and the methodological choices made by various investigators. As there is not a clear basis for choosing one set of studies over the other, the HES recommends that the Primary Estimate be derived as an intermediate value between the multi-city studies and the meta-analyses. The uncertainty distribution can then reflect methodological uncertainties as well as the uncertainties reported within individual studies.

Elaborating on this point, on page 2-9 the report indicates that the mean of the estimates derived from the three meta-analyses and the mean of the estimates derived from the three NMMAPS-based studies will be presented. However, the Primary Estimate is instead derived from a pooling of a 95-city NMMAPS-based study (Bell et al., 2004) and a 14-city case-crossover study not directly tied to NMMAPS (Schwartz, 2005), without weight on the other NMMAPS-based study (Huang et al., 2005) or the three meta-analyses. It would be better to present a Primary Estimate reflecting an intermediate value among the multi-city studies and the meta-analyses, with explicit consideration of the full body of evidence.

The uncertainty analyses presented in Exhibit 4-4 of the uncertainty report raised additional questions regarding the CRFs chosen and their rationale. For example, the Schwartz (2005) paper reported a 0.23% increase in mortality per 10 ppb increase in 1-hour maximum ozone concentrations. Using these same metrics, Bell et al. (2004) reported a value of 0.34%, yet the mortality incidence estimate in Exhibit 4-4 was lower. This could be explained if the Section 812 Prospective Analysis used the one-week average ozone findings from Bell et al. (2004), but this goes against the stated averaging time preferences in the report. Similarly, the three meta-analyses report corresponding values of 0.34%, 0.39% and 0.41%, but the incidence estimates are substantially greater for these meta-analyses than for the multi-city studies. More information about the CRFs derived from each study (and the assumptions regarding averaging times) would help to clarify why the benefits estimates appear to vary more substantially than the original studies, and in general, efforts to choose CRFs consistent with this full body of literature would be supported.

The HES notes that ‘attributable deaths’ as estimated using cohort mortality evidence (from long-term exposure) for PM and time-series mortality evidence (from short-term exposure) for ozone have potentially very different implications in loss of life expectancy, with mortality from long-term exposure likely to be much more significant. The HES is concerned about the implications for the economic valuation of mortality. In line with other guidance, EPA has adopted a VSL approach (as opposed to a life-year approach) within the Section 812 Prospective Analysis. The VSL approach treats all deaths as equivalent, irrespective of whether the associated loss of life expectancy is large or small. While accepting that this is standard practice, some HES members see it as counter-intuitive. The HES asks that EPA spell out, clearly, the assumptions underlying its valuation methods, and in particular why the average extent of life expectancy is considered irrelevant despite differences in method (time series vs. cohort), age, or other matters, so that readers can better understand the Benefits method and results. In addition to differences by age in life-years lost, the HES accepts that because economic valuation of life-years would not likely be constant with age, it is not immediately obvious to what extent differential values should be applied to time-series vs. cohort mortality evidence. This should be addressed within the valuation uncertainty analysis, which was not provided to the HES for review.

#### **4.6. Ozone Cessation Lag**

Agency-supplied background: Based on a perceived lack of empirical data to support specification of a cessation lag structure for ozone-related mortality effects, the Project Team has not attempted to apply a cessation lag structure for the Primary Estimate of ozone mortality reduction benefits in the draft benefits report, and alternatives are not evaluated in the draft uncertainty report.

Charge question 2f: Does the Council HES support the use of a no-lag assumption for the Primary Estimate of ozone mortality benefits presented in the draft benefits report? If not, are there methods for estimating and applying a cessation lag structure for ozone mortality that the Council HES recommends EPA consider, either for the Primary Estimates or for presentation in the draft uncertainty report?

HES response: The HES concludes that time-series data should be used for the Primary Estimate for ozone mortality. Time-series studies investigate health conditions or effects in a given cohort over time. Therefore, any lag in cessation of effects is already accounted for by the studies, and no further adjustment for cessation lag would be appropriate. The HES therefore supports EPA's position regarding cessation lag.

If Alternative Estimates are derived using cohort mortality evidence, there is no evidence in the literature to support a different cessation lag between ozone and particulate matter. The HES therefore recommends using the same cessation lag structure and assumptions as for particulate matter when utilizing cohort mortality evidence for ozone.

#### **4.7. Ozone Mortality Effect Threshold**

Agency-supplied background: Based on a perceived lack of empirical data to support application of a concentration threshold for ozone-related premature mortality effects, the Project Team did not attempt to apply an effect threshold for the Primary Estimate of ozone mortality reduction benefits.

Charge question 2g: Does the Council HES support the use of a no-threshold model for generation of the Primary Estimates of ozone mortality incidence reduction? If not, are there methods for estimating and applying an effects threshold, which the Council HES recommends EPA, consider, either for the Primary Estimates or for presentation in the draft uncertainty report?

HES response: The HES supports the use of a no-threshold model for ozone and mortality. The current scientific literature does not support a population-based threshold, as studies have found no supporting evidence for short-term exposure and only suggestive evidence for long-term exposure. For example, time-series analysis of ozone and mortality in 98 U.S. urban studies examined four model structures for the concentration-response curve: linear; subset; threshold; and spline models (Bell et al., 2006). All findings support the application of a no-threshold model, and also support the traditionally used shape of the concentration-response curve. Associations between ozone and mortality were present at low concentrations, nearing natural background levels. If a threshold for short-term ozone exposure and mortality exists, it is likely below the range of regulatory interest.

With respect to increased mortality risk from long-term ozone exposure, there is inconclusive evidence that a threshold may be present. A study of long-term health effects of ozone in 96 U.S. metropolitan areas for almost 450,000 persons for the ozone season (April to September) identified an association between ozone and respiratory-related mortality (Jerrett et al., 2009). A threshold analysis included a model in which a linear relationship between ozone and respiratory-related mortality risk is assumed for ozone levels above the specified threshold, and no association is assumed for levels below the threshold. Model fit was improved under the threshold model, compared to a no-threshold model (p-value 0.06), providing weak evidence of a threshold at 56 ppb daily maximum ozone concentration. Given this limited evidence for a threshold, the HES recommends that analyses based on findings from this study be conducted

both with the no-threshold model and with an assumed threshold model, as an alternative analysis.

#### **4.8. Baseline Incidence / Prevalence Estimates**

Agency-supplied background: Baseline incidence / prevalence are key determinants of the estimated changes in health effect incidence described in the draft benefits and uncertainty reports.

Charge question 2h: Does the Council HES support the choices made by the Project Team regarding baseline incidence / prevalence across the various human health endpoints incorporated in the Primary Estimate of benefits? If not, are there alternative baseline incidence / prevalence data which the Council HES recommends EPA consider, either for the Primary Estimates or for presentation in the draft uncertainty report?

HES response: The HES generally supports the choices made by the project team regarding baseline incidence/prevalence across the various human health endpoints. The HES recognizes that many of these choices are judgments within significant data constraints, and that the projected estimates have substantial uncertainties. The most important data, in terms of driving the benefit estimates, are the baseline mortality data, which are of relatively high quality. There is some concern about the noise and inconsistency in data used to estimate baseline school loss and work loss days. There may be too much noise to make reasonably reliable quantitative estimates of air pollution work loss days.

#### **4.9. PM Differential Toxicity Sensitivity Analysis**

Agency-supplied background: In its review of the Second Prospective Study analytical blueprint, the Council recognized that the state of the science did not support development and application of assumptions regarding the potential differential toxicity of PM components suitable for informing the present analysis. However, the Council did encourage the Project Team to explore the feasibility of conducting a sensitivity analysis to gauge the potential significance of differential toxicity. After extensive review of the literature and analysis of options, the Project Team concluded that currently available data and methodologies remain insufficient to meet the challenge of developing a reasonably valid and usefully informative sensitivity analysis, even on a notional basis. Indeed, the Project Team concluded that the potential research utility of such a sensitivity analysis in the end did not appear to justify the risks from potential misinterpretation and misapplication of the results of such a sensitivity analysis. The Project Team's evaluation of the issue of differential toxicity is presented in chapter 5 of the draft uncertainty report.

Charge question 2i: Does the Council HES support the Project Team's decision to defer quantitative sensitivity analysis of potential PM component differential toxicity? If not, are there data or methods for conducting a quantitative analysis of PM component differential toxicity that the HES recommends EPA consider, or are there other aspects of differential PM component toxicity which the HES recommends should be addressed in the draft benefits and/or uncertainty reports?



HES response: The Council had encouraged the EPA Project Team to explore the feasibility of conducting a sensitivity analysis to gauge the potential significance of differential toxicity. The Project Team has determined after a review of the literature that the currently available data are insufficient for developing an informative sensitivity analysis.

The Uncertainty Analysis document objectively reviews the evidence for various components, although research beyond 2007 does not seem to be included. Several recent papers could be reviewed (e.g., Ostro et al., 2007, 2008; Smith et al., 2009). The Project Team found a limited but growing literature addressing the health effects of various PM components, including (but not limited to) sulfate, nitrate, elemental carbon, organic carbon, and metals. They conclude that none of the components show consistently greater effects than PM as a whole; however, the epidemiological evidence base was clearly limited by the high correlations among many PM components (and between those components and PM as a whole). The Project Team concluded that “for this evidence base to be applicable to a differential toxicity analysis, it would need to be able to provide quantitative CRFs for all of the key components, derived in a manner so that the total reflected the observed effects of PM<sub>2.5</sub> and so that the estimates reflected possible interactions among components.”

The HES agrees that the evidence base at this time does not currently support this sort of assessment. Additionally, the HES finds that differential assessment – even if feasible – would not lead to substantially different results in an assessment such as the 812 Analysis, which deals with changes in the pollution mixture as a whole; and so it supports EPA’s decision to omit differential toxicity from the present 812 analysis. However, the HES recognizes that benefits analysis of specific measures may affect particular constituents of PM only, and that – for other analyses – the issue of differential toxicity should be considered anew.

#### **4.10. Dynamic Population Modeling**

Agency-supplied background: Chapter 7 of the draft uncertainty report describes the results of the Project Team’s application of a dynamic population simulation model to the evaluation of changes in pollution-related premature mortality risks. The Project Team continues to consider the potential utility of dynamic population modeling approaches and respectfully requests that the HES review the methodology and results and consider providing advice regarding the potential utility of further development and future application of this approach.

Charge question 2j: Does the Council HES have recommendations regarding the potential value for future analyses of the dynamic population approach described in chapter 7, or any alternative approaches the HES may suggest for addressing the issue of population changes during a study’s reference period?

HES response: The HES appreciates the work EPA has done to illustrate the use of dynamic population modeling for estimating the mortality impacts of long-term exposure to PM<sub>2.5</sub>. In general, HES supports the use of dynamic population modeling where practicable because it provides the most realistic available modeling of how, over time, changes in population risk lead to changes in the size and age distribution of the population, with consequent implications for estimated mortality impacts, whether expressed as deaths or life years.

We note EPA's concern that a full dynamic population implementation requires detailed projections for every year up to 2020 (compared with currently for 2000, 2010 and 2020 only), and that this is very resource-intensive if carried out at the small spatial scale of the current core methods. EPA should focus its dynamic population modeling on estimating mortality effects forward in time using one-year changes in exposure, based on the years 2000, 2010 and 2020 (i.e., the approach reported by EPA in the Uncertainty Report), when comparing dynamic population modeling with core BenMap methods. As noted by EPA, this is an intermediate strategy, which for a modest increase in effort captures many (though not all) of the gains of dynamic population modeling.

The HES discussed how the dynamic population approach highlights some subtleties in how monetary values are linked with the mortality implications of different pollution scenarios. HES requests EPA to describe, in substantially more detail than at present, the methods used, and the reasons why these methods rather than others were selected. This includes, but is not limited to, describing (1) the current ('static population') BenMap approach to estimating deaths postponed; (2) how, within this approach, VSL values are linked with changes in risk or deaths, and the assumptions underlying this approach; (3) why EPA favors valuation based on deaths / VSL rather than life years / VSLY; (4) whether EPA can link monetary values to the results of dynamic population modeling, and if so how this might be done; and in particular (5) whether the changing year-on-year pattern of deaths, illustrated by dynamic population modeling, can be incorporated into the monetary analysis.

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## APPENDIX A: Technical Corrections from Individual Members

The Subcommittee's advice and responses to the charge questions are contained in the body of this report. However, in the course of the review, the following technical issues were noted in the materials provided by the Agency. This is not intended to be an exhaustive list.

### **Regarding the health benefits chapters from the draft *Health and Welfare Benefits Analyses to Support the Second Section 812 Benefit-Cost Analysis of the Clean Air Act* (dated November 2009):**

P. 1-6: It appears that the primary benefits result includes CAIR, but this has not yet been promulgated, and would not have influenced the year 2000 benefits in any event. It is later mentioned in the qualitative uncertainty analysis that the issue of assuming CAIR when it is not yet in place is a potentially major uncertainty, but it would be nice to provide even more insight about this question (since CAIR itself has been associated with benefits of \$70B in 1999 dollars and using some other "older" assumptions). Doing new runs assuming no CAIR is impractical, but this should be able to be quantified at first order given the previous RIA of CAIR.

P. 2-7, Exhibit 2-2: It is not clear why "low birth weight" is not quantified; it is a birth outcome which has long lasting impacts on development. Are there too few studies from which reliable estimates can be derived? Some mention of the decision for this outcome should be included in the text or as a footnote to this exhibit.

P. 2-8, Exhibit 2-3, footnote a: In the last sentence "biological similarity" is puzzling. Children between the ages of 5 and 17 continue to develop biologically, including in the nasal-respiratory tract. Is EPA saying that the NRC determined that the differences in respiratory system developmental stages for ages 5-17 were not significant for estimating PM-related health effects? Please clarify or correct this statement; as currently written it is too vague and broad.

P. 2-10: It is not true that the individual time-series studies either used 24-hour average or 1-hour maximum levels for exposures; multiple studies did use 8-hour maximum. For example, Fairley (2003), Klemm (2000), Michelozzi (1998), Saez (2002), Anderson (2001), Bremmer (1999), Roemer (2001) all used 8-hour maximum. These studies (and probably others) are embedded in the meta-analyses.

P. 2-12, School absence section:

The recommendation from the NRC should be briefly stated so the reader can understand the justification for extending the cited studies to a wider age range. Further, in the last sentence of this section the logic used for deriving the estimate should be expanded.

P. 2-15: It seems strange to argue that there is an extensive body of literature on CHA and RHA and then to choose only 2 studies for the estimates. Why not use, for example, the meta-analyses conducted in Europe in 2006 by the Committee on the Medical Effects of Air Pollutants, which pooled 50+ studies of CHA in a very careful manner?

P. 2-17 to 2-18, Baseline Incidence Rates section:

The title for this section does not match that of the related exhibit. More importantly, some of the data sources and their limitations are not described in this section. For example, the “School Loss Days” database parameters (e.g., ages covered) and challenges in using them are not included in the text.

P. 2-18, last paragraph: The discussion of the asthma prevalence rates and assumptions needs to be clarified. Does “in future years” refer to post-1999 (e.g., after the ALA data), or from 2009 based on 1999, or something else? It is not clear whether the basis for the “current trends” in the first half of the last sentence is the study cited or whether another study and/or national database (Ostro et al, CDC, ALA, etc) was/were used for this comment. Further, a trend requires at least two points in time; what were those points? There is no recognition of whether rates have been affected by changes in diagnostic, treatment and/or reporting practices that may affect predicted rates. Last, the 4% chosen may be relevant for the 2020 national population but not for at-risk subpopulations, such as those noted in Exhibit 2-6. Are demographic changes in these subpopulations expected to result in overall population prevalence rates that would exceed 4%? Clarification of these several issues would help the reader understand the bases for and therefore the validity of the asthma data used and the 2020 prevalence rate assumption.

P. 2-20: Exhibit 2.5. Baseline Incidence/Prevalence Rates

- In the first row (Mortality), the scope and years of data used should be clarified further. Because “infant mortality” was not specified as a row item, it was not clear to this reviewer whether infant mortality data were included. Wonder includes infant mortality data for 1995-2005; were any of these data (or only 1996-1998?) used to derive the risk estimate for the “< 18” rate? If infant mortality data were included, the Mortality row needs to include an “infant mortality” line for the data source and years of data used. If not, the ages for the “< 18” column need to be clarified.
- In the row marked “School Loss Days,” the National Center for Education Statistics (1996) database is cited. However, this data source is not easily located on the Internet. The citation for this database is currently missing and needs to be listed in the References section of this chapter.

P. 2-27 and Exhibit 2.14: This reviewer assumes that “School Loss Days” on p. 2-27 became the “Work Loss Days” in the exhibit. Clarify in the text whether this is the case or not. Further, if “Work Loss Days” includes several endpoints, then all of the inclusions should be clearly stated.

P. 2-29 to 2-31: Applying the eyeball test, it seems strange that mortality incidence is about 3-4 times higher at the mean than the 5<sup>th</sup> percentile, while valuation is about 70 times higher. This patterning doesn’t exist for morbidity endpoints or for PM mortality, and the text did not mention (that I noticed) any use of lower valuation for ozone mortality even as a bounding calculation.

**Regarding excerpted materials from the draft *Uncertainty Analyses to Support the Second Section 812 Benefit-Cost Analysis of the Clean Air Act* (dated November 2009):**

P. C-8: I'm not sure if I agree with some of the "major/minor" conclusions drawn in Table C-4. For example, the exclusion of populations under 30 from the mortality health impact assessment will have a trivial effect on the risk calculations, given the very low baseline mortality rate in these populations. It seems unlikely that the exclusion of air toxics has a potentially major effect on the net benefit estimate, as previous studies have shown air toxics cancer risks to be orders of magnitude less than criteria pollutant risks. The two ozone mortality incidence estimates that were pooled were from the same study and differed minimally, so this would not be a major effect.

P. C-8-11, Table C-4: The rationale for the choice of health effects and their related uncertainties documented in this table are not apparent. While adult mortality-related assumptions and uncertainties must be described because they drive the overall estimate, the table also presents information about an adult morbidity factor. Chronic bronchitis (the second most important contributor to the overall estimate) is included in the table, but there is no mention of "nonfatal myocardial infarction," which is another morbidity outcome and a close third contributor to the health effects estimate. Additionally, there is no mention of infant mortality or other childhood health effects.

Whether the purpose of this table was to capture the "key uncertainties" for the top three contributors to the health estimate or for adult outcomes only, there are inconsistencies within either scope. The rationale for the choice of health effects and their related uncertainties documented in this table should be clearly stated in supporting text.