Responses to CASAC Questions about the Draft PM PA
from Consultant Dr. Duncan Thomas

Before answering the specific questions posed by chairman Dr. Tony Cox and other members of CASAC, I'd like to offer some general observations.

First, I have reviewed substantial portions of the draft PA, focusing particularly on my area of expertise, Chapter 3, as well as some parts of the External Review Draft ISA dated October 2018 and the CASAC Draft Report (03/07/19) to Assist Meeting Deliberations. In general, I find both the draft PA and the draft ISA to be well written, authoritative, and comprehensive reviews of the literature and thoughtful discussion of the policy implications, including limitations thereof. Two main themes seem to me to emerge from the questions that Drs. Cox and Lange have posed, and as reflected in the CASAC critique of the ISA.

The first is an emphasis on the difference between association and causation, as discussed in the epidemiologic literature for well over a half century, and the limitations of epidemiologic evidence for drawing causal conclusions. In the last couple decades, this has spurred the development of novel methods of "causal inference", i.e., statistical methods for analysis of observational data to address the expected changes in outcomes that might result from hypothetical changes in exposures (often called the Average Causal Effect). Despite the growing interest in such approaches, they have only recently been applied in the field of air pollution epidemiology (e.g., (Moore et al. 2008; Moore et al. 2010; Zigler et al. 2012; Wang et al. 2016; Zigler et al. 2018)). These are important contributions with direct policy applicability, but the vast majority of epidemiologic studies report standard measures of association (e.g., relative risks, etc.). This is not to disparage the bulk of epidemiologic studies, only to emphasize that it would be inappropriate to dismiss them as not addressing causation, given their concordance and the general conformity with the criteria used by epidemiologists for decades to qualitatively evaluate causation.

The consultants received a list of additional citations by Dr. Cox on 9/24/19 about his views on causality. These were provided as background, but the consultants were not asked specifically to comment on them. I have not read these four papers, although I have read others by him on this topic, have peer-reviewed one of them in detail, and am generally familiar with his views. If requested, I can review them and elaborate further, but the main points are covered in the responses to the questions below.

The second recurring theme is an emphasis on uncertainty. All scientific evidence — observational or experimental — is always fraught with some measure of uncertainly, generally addressed qualitatively in the Discussion section of scientific papers and quantitatively in terms of such statistical measures as standard errors of estimates, measurement error adjustments, etc. Air pollution epidemiology is no exception. Critical reviews of the literature and quantitative meta-analyses pay particular attention to both quantitative measures of uncertainty as well as judgments of study quality, potential bias, etc. In this regard, my impression from what I've read of the draft ISA and PA documents is that the authors have done an excellent job of addressing these uncertainties and their policy implications.

I will elaborate on these general points in responding to the specific questions from CASAC members below. I am limiting my answers to a subset of the questions that are closest to my area of expertise in biostatistics methods, rather than the substance matter of air pollution epidemiology (with which I have some familiarity from my work in the field for about 25 years, but would not consider myself having the comprehensive knowledge of a substance matter expert).

<u>Questions from Dr. Anthony Cox</u> [edited for brevity]

Are the C-R models in Table C-1 appropriate, logically valid, and empirically well-validated, for answering the causal question of how changes in PM2.5 levels would change health risks? Both specific and general versions of this question are of interest:

- *Are the specific regression models in Table C-1 known to produce valid predictions or simulations of how changing PM2.5 exposure would change population health effects or risks?*
- *In general, are such regression models appropriate for predicting how an intervention or manipulation that changes the value of a predictor (right-hand side variable) would cause the value (or frequency distribution) of the dependent variable to change? If certain conditions must hold for this to be an appropriate use of regression models, what are they, and has the PA shown that they are satisfied for the C-R regression models in Table C-1?*

RESPONSE: These general questions are adequately covered in my responses to the specific questions below.

1. Are the beta coefficients in Table C-1 of the PA conceptually well defined? That is, are their intended conceptual meanings and causal interpretations clear and unambiguous? If so, can the definition of beta be expressed using standard epidemiological terms (e.g., controlled direct effects, natural direct effects, total effects, indirect effects, and so forth?) [references omitted]

RESPONSE*:* The "standard epidemiological terms" mentioned in the question relate to mediation analysis, which is not relevant here. If the goal were to assess whether the effects of air pollution on mortality were mediated through some intermediate variable (say, inflammation), then the natural indirect effect would describe the effect of the pathway pollution → inflammation → mortality; the natural direct effect that of pollution → mortality through mechanisms other than inflammation; and the total effect the sum of the two. Likewise if the goal were to assess the effect of socioeconomic effect on mortality through air pollution, the indirect effect would describe the pathway socioeconomic status → pollution → mortality; the direct effect that of socioeconomic status on mortality through mechanisms other than pollution; and the total effect the sum of the two. In either case, the terms refer to the expected causal effect of some intervention. For example, Zigler et al. (2012) partition the average causal effect of a hypothetical intervention to regulate air pollution into "associative" and "dissociative" components: regulation that has an effect in areas where it causes improvement in air quality, vs regulation that improves mortality without reducing pollution, e.g., through some other mechanism such as changes in unemployment.

Other than the handful of references cited above, most epidemiologic analyses report measures of association, such as relative risks, or derived quantities such as the change in relative risk per unit change of exposure. These are well defined quantities, although they lack a direct causal interpretation (more on this below).

*2. On the same topic of clear definitions, does the discussion of the BenMAP-CE beta coefficients in the PA and underlying documentation (*described *as typically representing "the percent change in a given adverse health impact per unit of pollution") unambiguously specify which of the following concepts the coefficients represent?*

a) Beta estimates the percent change in the conditional expected observed value of the health impact associated with a unit change in the observed value of the pollution variable. …

b) Beta estimates the percent change in the mean value of the health impact variable caused

by a manipulation or intervention that changes the value of the pollution variable by 1 unit …, while holding the values of all other variables fixed at the values they had before the intervention. …

c) Beta estimates the percent change in the mean value of the health impact caused by a manipulation or intervention that changes the value of the pollution variable by 1 unit … , while allowing the values all other variables to change in response to the changes in pollution. …

d) Beta estimates the percent change in the mean value of the health impact caused by a manipulation or intervention that changes the value of the pollution variable by 1 unit … , while holding the values of all other variables … fixed at the values they would be expected to have after the intervention.

e) Beta means something different from any of the above.

Do all of the beta values in Table C-1 refer to the same one of these concepts, or might they refer to different ones (or is the answer not clear)?

RESPONSE: Choice a) would be close, except that it lacks the qualification (except as implied by the word "conditional") provided in choices b) through d) that all other variables are held constant, so I suppose the correct answer would be e) something different. Choices b) through d) are not appropriate because in most analysis of observational epidemiology there is no intervention being studied. Instead, beta coefficients (and the risk estimates from which they are derived) represents a form of weighted average of the observed association between exposure and outcome within strata defined by levels of all other variables. That said, the usual interpretation is that it represents the expected reduction in an individual's risk of the outcome if exposure had been reduced by one unit, holding everything else in the regression model fixed. The expected value of a regulation that would affect the distribution of exposures in a population on health outcomes can be derived from the beta coefficients using the techniques described in the PA. Since, to my knowledge, none of the studies described in Table C-1 are intervention studies, the beta coefficients given would all have the same "regression interpretation".

3. *Similarly, is the definition of "concentration-response (C-R) relationships" in the PA and its Appendices (cf p. C-38) adequately clear and unambiguous to support simulation of well-defined causal effects of interventions that change pollution levels? …*

RESPONSE: Yes, clear and appropriate for use in the simulation of the effects of hypothetical interventions.

4. … Do the beta coefficients in the PA overcome these methodological objections to using relative risks, regression coefficients, and related measures of association to predict (or simulate) effects of interventions? If so, how were they overcome? If not, does this imply that the simulations in the PA are not necessarily reliable or valid predictors of the real-world effects on public health of reducing PM2.5? Why or why not?

RESPONSE: I don't believe there are serious methodological objections to the use of such measures of association for the purpose of risk assessment, so nothing to overcome. The simulations in the PA appear to me to be valid.

5. *… which, if any, of these measures (relative risks, odds ratios, attributable risks, and regression coefficients) are currently generally accepted in contemporary causal analysis and epidemiology as valid measures of how changing one variable (e.g., exposure) will cause another (e.g., population health*

responses) to change? …

RESPONSE: All these epidemiologic measures of risk are widely accepted as valid measures of the association between differences in exposure and outcomes across individuals (in the case of cohort studies) or of the association between differences in exposure and disease rates in a population across time (in the case of time series studies). Their causal interpretation as the expected effect of a hypothetical intervention to change exposure (among individuals or across a population) requires additional assumptions, but these may be reasonable depending on the context.

6. More generally, do the $\Delta y/\Delta x$ values calculated by BenMAP-CE have valid interpretations as causal impacts on y of interventions that change x? …

RESPONSE: Same response as to question 5.

7. Have the beta coefficients in the PA been empirically validated as providing approximately correct or usefully accurate predictions or simulations of how interventions that change air pollution would change population health responses? … To what extent are such findings [from a recent non-EPA review] from actual interventions consistent with the assumptions, confidence intervals, and simulations in the PA?

RESPONSE: Same response as to question 5. I am aware of various quasi-experimental ("accountability") studies of the health effects of changes in air pollution but am not in a position to be able to compare their estimates quantitatively with those from purely observational studies. This seems to be the closest one could hope to come to "empirical validation" of risk reduction predictions.

8. Does the discussion of beta values in the PA, including the discussions of uncertainty, confidence intervals, and sensitivity analyses, adequately describe and discuss the extent (if any) to which their values reflect potential omitted confounders of the association between mortality risks and PM2.5 levels …

RESPONSE: I found the discussion of these points in the PA to be thorough and well-reasoned. Uncontrolled confounding can never be eliminated in any observational study; the best one can do is control for known measured confounders. The same could be said of causal inference analyses of observational data. Only randomized experiments can eliminate confounding (both known and unknown) and then only in expectation, and this is not feasible for air pollution studies for obvious reasons.

9. Does the discussion of beta values in the PA, including the discussions of uncertainty, confidence intervals, and sensitivity analyses, adequately address the extent (if any) to which their values reflect residual confounding of the association between mortality risks and PM2.5 levels…

RESPONSE: Same as for question 8.

10. Does the discussion of beta values in the PA, including the discussions of uncertainty, confidence intervals, and sensitivity analyses, adequately address model uncertainty (e.g., the possibility that the linear no-threshold model specification is incorrect…)?

RESPONSE: Yes, but worth elaborating. The observed range of risks is generally very small, albeit frequently highly significant because of the large sample sizes. Over this range, differences in the shape of the C-R relationship are virtually indistinguishable. Any C-R function can be approximated by a Taylor series, of which the first term describes the slope of the relationship at zero exposure (Crump et al. 1976);

if nonzero, then there is no "threshold" below which there is absolutely no effect (even if very small). Statistical methods are available to test for nonlinearity (as described in chapters 6 and 15 of my environmental epidemiology textbook (Thomas 2009)), including the existence of a threshold and inter-individual variability, but when the range of risks is small, such methods have very low power.

11. Does the PA's discussion of beta values, including the discussions of uncertainty, confidence intervals, and sensitivity analyses, adequately address effects on the estimated values of the beta values of exposure uncertainties and estimation errors…?

RESPONSE: Yes, same as for question 8.

12. Does the PA adequately assess the suitability of the designs of the studies used to estimate beta values for purposes of valid causal inference and simulation? Does the PA's discussion of uncertainty and sensitivity analyses adequately address the internal validity and external validity (generalizability) of the estimated beta values used to simulate the causal impacts on public health risks of changing PM2.5 levels?

RESPONSE: Yes, the cohort and time series study designs used to assess chronic and acute effects of air pollution are standard in the field and widely accepted as providing valid estimates of association parameters. There relevance for estimating the average causal effect of hypothetical interventions has been addressed above. The response to Dr. Cox's queries by Dr. Vandenberg dated 2/20/19 cogently explains why such hypothetical questions are beyond EPA's mandate.

13. Does the PA's discussion of beta values adequately address attribution of risk in the presence of joint causes? … Conversely, how well does the discussion in the PA make clear how much of the estimated beta value for PM2.5 is actually contributed by other variables … that would not necessarily be changed by an intervention that reduces PM.5 levels?

RESPONSE: Yes. See my response to Dr. Lange's question 5 below for further details.

14. Overall, does the PA and its underlying documents (e.g., the BenMAP-CE documentation) make a convincing technical case that its simulated health impacts of reductions in PM2.5 are trustworthy and usefully accurate? How confident can policy analysts and decision makers be in the predictive validity of the simulated results?

RESPONSE: Yes.

15. Are there other statistical or methodological issues that you would like to comment on that you believe might help the CASAC to assess the validity and soundness of the PA and its simulations for effects on health risks of changing PM2.5 levels, or that might help to improve the technical and scientific quality of the final PA?

RESPONSE: No nothing further.

16. How can techniques of formal causal modeling and analysis best be applied to improve the clarity of definitions and communication and scientific soundness of simulations, inferences, causal interpretations, generalizations, and policy-relevant conclusions in the PA? …

RESPONSE: Formal causal inference methods do indeed have a potentially important role in the future,

as exemplified in some of the references cited above, but at present very few studies have exploited them. Without access to the raw data, it would not be reasonable to expect others conducting meta-analyses (e.g., EPA staff) to reanalyze published studies using these techniques (which is not to say that studies for which raw data are not accessible — e.g., for appropriate human subjects reasons — should be excluded).

Questions from Dr. Sabine Lange [edited for brevity]

1. Is it appropriate to compare daily PM2.5 concentrations to the annual average? .... The concentration-response functions in the short-term epidemiology studies are derived using day-to-day changes in PM2.5, which doesn't seem like it would be captured in an overall average concentration…

RESPONSE: I'm not sure I understand this question. Obviously, there is no reason to expect that acute effects of short-term fluctuations would be similar to the chronic effects of long-term exposure (Kunzli et al. 2001; Thomas 2005). On the other hand, it would not be unreasonable to wonder whether the magnitude of acute effects might differ depending on the long-term average level of pollution. Since the daily variation and long-term average are on different scales, it would be reasonable to use different values to assess them.

2. Is it informative to derive annual average pseudo-design values for study areas in short-term studies …, in order to determine whether these study areas attained the current annual standard? Although the EPA can technically determine if daily changes in PM2.5 concentration increased health effects in an area meeting the annual standard, does this really inform the health protectiveness of the annual standard? It seems that whether an area showed a positive effect or not could be completely independent of the annual standard and instead dependent on how much the PM2.5 concentrations changed from day-to-day.

RESPONSE: Both are possible, as discussed in my response to the previous question.

3. In contrast to short-term studies that investigate the effects of day-to-day changes in PM2.5 concentrations within a certain geographic area, long-term cohort studies often look at the association between annual average PM2.5 concentrations and time-to-event ... over long periods of time. ... In this case, is the pseudo-design value in a single geographic area particularly informative, when the association between PM2.5 and the health effect is driven by the differences between study areas?

RESPONSE: Yes, indeed, it is precisely the differences between study areas that is most important for estimating long-term effects. For reasons discussed above, such association effects are not strictly interpretable as causal effects of an intervention, hence the use of these "pseudo-design" values for simulating the expected effects of regulations to change the distribution of exposures.

4. Is there a quantitative uncertainty analysis method that the EPA could use for this risk assessment that captures more of the uncertainty and variability of the risk estimates …?

RESPONSE: There certainly are methods of uncertainty analysis that can be applied to the analysis of original epidemiologic data, were it available, but this would generally be beyond the capability of EPA staff without access to raw data (see my response to Dr. Cox's question 16). The simulations based on epidemiologic risk estimates used by EPA do address such uncertainties and variability, to the extent possible in meta-analysis.

5. Could different magnitudes of error amongst different variables in regression analyses be masking the effect of a speciated constituent of PM2.5?

RESPONSE: Yes, in principle. It has been well known that measurement errors in one variable can bias the estimates of the effect of another variable (Zeger et al. 2000). The magnitude and direction of this bias depends on the correlation of the two variables and of their measurement errors, as well as the strength of the true effects of both variables. While the various pollutants may be fairly highly correlated, their measurement errors are likely to be less so, and two-pollutant models including, say, PM2.5 and a gaseous pollutant are still likely to be relatively robust and better than ignoring the co-pollutant. PM species are typically more difficult to disentangle and have seldom been incorporated simultaneously in multi-pollutant models.

6. What happens when multiple potential explanatory factors are included in a single variable in an already-complex multiple regression system? What kind of an impact would this inclusion of multiple potential explanatory factors into one variable have on the final C-R function, and how accurate would that C-R function be?

RESPONSE: This depends upon the degree of multi-colinearity among the variables in the regression equation. The general effect of adding too many highly correlated variables is to inflate the standard errors of the estimates rather than introduce any bias (except in certain conditions, as described in my response to question 5). Adjusting for confounders such as contextual variables (e.g., socioeconomic status in a cohort study of chronic effects) or temporal variables (e.g., weather in a time series study of acute effects) is unlikely to lead to substantial inflation of standard errors and is necessary to control for confounding. On the other hand, multiple pollutants tend to be fairly highly correlated, particularly for constituents of PM. Hence, few epidemiologic studies of either types have attempted to include more than two pollutants in the same model, and then only to assess the extent to which estimates of the effect of one pollutant are affected by inclusion of the other. Novel statistical methods that allow smoothed estimation of multivariable effects such as Bayesian Kernel Machine Regression (KMR) have become popular for analyzing high-dimensional genomic and other data, but have only recently been applied in air pollution epidemiology, e.g., (Bobb et al. 2014).

Questions from Dr. Mark Frampton (edited for brevity)

1. Is there evidence that would support a reconsideration of the current and long-held views of this causal relationship as expressed in the PA and ISA?

RESPONSE: In my view, none of the new epidemiologic studies would alter the fundamental approach EPA has been using to assess the causality of air pollution health effects, although estimates of the magnitude of effects may be strengthened by new data, particularly on the question of effects below the current standards. (More on this in response to question 3).

2. In the long-term epidemiological studies of PM mortality, heterogeneity between and within cities has been cited as a source of uncertainty in drawing conclusions about causality. Please opine on the level of uncertainty that is represented by this heterogeneity, and the impact if any, on the conclusions in the PA.

RESPONSE: Heterogeneity between and within cities is to be expected and can be useful to explain, e.g.,

whether variation between cities is due to differences in pollutant mix, for example, or variation within cities is due to age, socioeconomic or health status, etc. Such factors are relevant to the EPA's mandate to protect the most vulnerable segments of the population, and the current PA adequately discusses these issues.

3. ... Please opine on the adequacy of the causality analysis framework currently used by the EPA, and whether and how the concepts espoused by Dr. Cox should, or should not, be incorporated into the NAAQS causality framework. Also please comment on the implications, of any changes in the causality framework that you would recommend, for the analyses and conclusions in this current PA.

RESPONSE: In my view, while modern causal analysis methods being developed in the statistical literature have potential utility in the future, they are not presently amenable to the kinds of reanalysis of primary data by EPA staff that Dr. Cox is calling for (see my response to Dr. Cox's question 16). The few examples of recent applications of such methods by investigators with access to the raw data that I am familiar with have been cited above and merit consideration and discussion in the PA.

4. The CASAC letter to the Administrator (April 11, 2019) states, "There is inadequate evidence for the 'likely to be causal' conclusion for long-term $PM_{2.5}$ exposure and cancer." This is based on epidemiological studies that do not appear to adequately differentiate incident cancer and cancer-related mortality because the exposure time frames for most of these studies are insufficient to draw conclusions about incident cancer. Do you agree with the CASAC's findings in this matter? Please discuss the evidence (or lack thereof) that supports your opinion.

RESPONSE: The challenge of establishing causal long-term effects of air pollution of cancer incidence or mortality are not fundamentally different. Cohort studies that are based on prospective follow-up of outcomes using only air pollution exposure information available at entry to the cohort would obviously require many years of observation, whether incidence or mortality is being studied. However, many cohorts are able to take advantage of the decades of air quality monitoring data that precedes the initiation of the cohort; those studies that have only place of residence at or since enrollment would obviously be subject to some degree of measurement error for those subjects who had moved previously, but some cohort studies have collected detailed residential histories that would allow comparisons within cities based on individual exposure histories. That said, the only fundamental difference between incidence and mortality is that data on the latter are more widely available on much larger populations, so there are many more such studies.

5. Please comment on the appropriateness and completeness of the approaches used in this PA to assess the risks of exposure, and the assessments of risk reduction of alternate standards, for $PM_{2.5}$ and PM_{10} (sections 3 and 4, respectively).

RESPONSE: I think my other comments here adequately address the first part of the question. I found the assessment of the implications of alternate standards to be a particularly interesting and compelling part of the report.

6. Are there additional key studies that should be considered in sections 3 and 4 of the PA?

RESPONSE: Not to my knowledge, but I do not consider myself a substance matter expert in epidemiology.

Questions from Dr. Steven Packham (edited for brevity)

1. Are there areas (e.g., specific aspects of biological causation, pulmonary toxicology, or causality in epidemiology) in which additional knowledge is required to appraise the adequacy and basis of existing, new, or revised PM NAAQS to protect public health with an adequate margin of safety?

RESPONSE: I can only speak to the field of epidemiology, which has been the workhorse for providing the evidence in support of NAAQSs. Obviously, such research is on-going and will continue to contribute to future risk assessments. The current ISA and PA adequately cover the current state of epidemiologic knowledge. Future efforts to characterize effects below the current standard, as well as the application of causal inference methods to analyze observational epidemiology data and "accountability" studies to evaluate the effects of actual changes in pollution in response to new regulations will be important in the future. Closer integration of experimental toxicology and observational epidemiology would also be helpful, as mentioned below.

2. Can you suggest additional specific scientific disciplines and areas of biomedical informatics and research (e.g., systems biology methods for clarifying biological causal pathways, mechanisms, modes of action, quantitative causal dose-response relationships) that should be included in future reviews of other criteria pollutants?

RESPONSE: Beyond the application of novel statistical methods of causal inference to epidemiologic data, methodological advances for studying mechanisms of action (systems biology, etc.) are out of my area of expertise. That said, I am aware of the excitement over -omics methods (metabolomics, etc., not just genomics) and am currently leading an NCI program project grant on "statistical methods for integrative genomics in cancer" which aims to develop such methods and am collaborating with my epidemiologic colleagues on applications to metabolomic data on air pollution.

3. Can you describe the research efforts necessary to provide the required information? To what extent has the needed research already been done, or started? For example, are there crucial experiments or research initiatives that could clarify the shape of the PM2.5-chronic inflammation causal dose-response relationships at relevant exposure concentrations? Are there specific data analyses (e.g., testing for confounding by weather variables over more days prior to mortality) that could clarify the causal interpretation of epidemiological associations relied on in the draft PA to simulate effects of interventions?

RESPONSE: See my responses to questions 1, 2, and 4.

4. Can you suggest additional areas of scientific literature review on species and individual human organism's capacities of adaptation to inhaled environmental stressors that might help establish margins of safety when exposed to ambient levels of air pollution?

RESPONSE: Generally beyond my expertise, other than to comment that there is growing interest in methods of formally integrating experimental animal and other mechanistic studies into the analysis of epidemiologic data (e.g., through hierarchical Bayes models).

5. Could you provide additional information on the relative contributions to air pollution concentrations and resulting health effects of natural and anthropogenic activity? For example, is either

one alone, or are both natural and anthropogenic activities together, sufficient to cause the magnitudes of adverse health effects attributed to PM2.5 in the Draft PA?

RESPONSE: Beyond my expertise.

6. Could you provide additional information on any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attainment and maintenance of such national ambient air quality standards?

RESPONSE: Beyond my expertise.

Questions from Dr. James Boylan (subset, Chapter 2 questions are outside of my expertise)

Chapter 3:

1. Is the evidence-based analysis presented in Chapter 3 scientifically sound?

RESPONSE: Yes, see comments above.

2. Is the risk-based analysis presented in Chapter 3 and Appendix C scientifically sound?

RESPONSE: Yes, see comments above.

3. Is the discussion on following topics adequate and complete? If not, what additional information needs to be included?

- *Study area selection,*
- *Health outcomes (e.g., decision to focus on mortality and ignore cardiovascular and respiratory effects),*
- *Concentration-response functions,*
- *PM2.5 air quality scenarios evaluated,*
- *Model-based approach to adjusting air quality,*
- *Linear interpolation/extrapolation to additional annual standard levels, and*
- *Characterization of variability and uncertainty in the risk estimates.*

RESPONSE: No further comments on any of these points beyond my responses elsewhere in this document. In general, I found the PA's treatment of these issues adequate and complete.

4. Are the areas for additional research adequate and complete? If not, what additional areas need to be included?

RESPONSE: See my response to Dr. Packham's questions 1-4.

Appendix C

1. Is the air quality modeling approach to projecting PM2.5 concentrations to correspond to just meeting the NAAQS (AQS, CMAQ, Downscaler, SMAT-CE, project monitors to just meet NAAQS, project spatial fields to correspond to just meeting the NAAQS) scientifically sound? If not, what are your concerns and how should they be addressed?

RESPONSE: Beyond my expertise

2. Is the CMAQ model configuration and input files used in the air quality modeling appropriate for this application? If not, what updates are recommended?

RESPONSE: Beyond my expertise.

3. Are the CMAQ model performance metrics that were evaluated appropriate and adequate for this application? Are there any concerns with the model performance in any of the study areas used in the human health risk assessment? If so, how should these concerns be addressed in the health risk assessment?

RESPONSE: Beyond my expertise.

4. Is the health risk modeling approach using BenMAP-CE appropriate for this application? If not, what are your concerns?

RESPONSE: While I am not personally familiar with the BenMAP-CE program, the description of the methodology in Appendix C seems clear and appropriate for this task.

5. Do the risk summary tables showing the impact of alternative PM2.5 standards and graphical plots showing the distribution of risk across ambient PM2.5 levels clearly and accurately summarize the results of the health risk analysis? If not, what additional information should be included?

RESPONSE: I found the presentation of the risks from alternative PM2.5 standards to be clear.

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