Response to CASAC Questions on the PM PA from Dr. D. Warner North
September 26, 2019

I have received questions from five CASAC members. I have had time to read much of the Policy Assessment, External Review Draft of September 2019, and also the CASAC letter report of April 11 and the Administrator's Reply of July 25.

I am providing a preliminary response stating my impressions based on my reading to date, with references to materials that I think CASAC members and other non-member consultants will find useful. I will welcome dialogue via e-mail among us. Part of my motivation for sending this response early is that I have a long-standing major commitment (a talk) on October 8, and I must spend much of my time between now and then preparing it rather than doing further reading and research as part of my recent engagement to help CASAC. But I believe we as a group will need to continue our dialogue via formal Questions and Responses, all made available to the public. The issues are deep. In my judgment, EPA's existing risk assessment process is in need of much correction from CASAC. That process has started with the review of the draft Integrated Science Assessment, and I can support most of what CASAC has already said in its April 25 letter. I also respect what the Administrator has said about meeting the deadlines. I welcome learning the views of others, and I reserve the right to change the opinions expressed below as I learn more.

The Questions from Dr. Steven Packham are among the most recent to arrive, so I will comment briefly on these first. I was going to start my response with a review of the charge to CASAC, and I am pleased to see his summary including the charge at the beginning of his Questions. I envision CASAC's main task as reviewing the scientific information and analysis supporting the revision of the numerical NAAQS standards for PM. But CASAC should also provide guidance on needed research and analysis methods (ii), and address the effects of various strategies for attainment and maintenance of NAAQS so as to protect public health (iv).

The historical context is important. I cannot claim to know it well by reading all five documents, but I think my background gives me the opportunity to offer evaluation and advice. Let me list three main themes before I get into the wording of questions.

I. EPA's determinations of causality seem to me seriously flawed by confounding. The confounding factors appear to be socioeconomic status (SES) and weather variables such as extremes of heat and cold. Using lay language, heat waves in summer result in increased mortality, and cold waves in winter result in influenza and other conditions leading to increased mortality and morbidity. Low-income and especially elderly and disabled people may be especially susceptible to these extreme temperature effects, so these factors are not readily separable.

II. Particulate matter is not one substance, but a mixture. It should be expected that since sources differ, the concentration- response (C-R) relationship may therefore differ from place to place. Further, there is important uncertainty in the shape of the C-R relationships, which may differ from place to place because of differences in sources, weather, atmospheric chemistry, and the exposed populations. Using the Cox proportional hazard model with national averaged data is essentially equivalent to assuming a single, linear-through-zero relationship, and it suppresses uncertainty and variability. The uncertainty should be made explicit. Epidemiological and other data addressing place-to-place variability should be sought and used. Some studies with such spatial heterogeneity have been recommended to

EPA by CASAC as additions to the ISA. More may be available or become available. Sensitivity analysis and weighting on C-R relationships at different concentration levels should be a useful supplement for EPA to include in its risk assessments. What EPA has done in Chapter 3 and Appendix C of the draft PA seems to me extremely simplistic, and potentially misleading on the extent of lives and disease that would be avoided by more stringent standards.

III. Fires, especially wildfires, contribute a large portion of fine particulate matter ($PM_{2.5}$) in the west and especially in California, the state in which I live. EPA should work with other federal agencies and state and local agencies to assess the public health consequences of fires and foster the development of strategies to reduce wildfires as a source of particulate matter air pollution.

Rather than organizing by charge questions and by the questions posed by the five members of CASAC, it may be most effective if I first develop these three main themes with references. Then I will respond to the CASAC questions.

Theme I. Causality and confounding. This is a major concern in the questions of Dr. Mark Frampton. Tony Cox has just sent out references to links to four of his papers. I have reviewed Tony Cox's book, *Causal Analytics*, and I was a reviewer for an earlier draft of his paper in *Critical Reviews in Toxicology*. I am in general agreement with Tony Cox on the importance of confounding, the need to consider the Bradford Hill Criteria as out-of-date, and the importance of obtaining data that will allow discriminating among multiple potentially causal factors.

My review of Tony Cox's Book and of two books by Judea Pearl is recommended as a starting point to those unfamiliar with this area of scholarship. Professor Pearl at UCLA is considered one of the pioneers of artificial intelligence methods in computer science, which are now very extensively used in information technology commerce, sometimes under the heading of data science. His *Book of Why* is an easy read and a good source of instruction on the limits of regression-based statistical techniques still in wide use. And I urge those on CASAC not familiar with this material to read the papers Tony Cox has sent out to the group, and as well as Pearl's *The Book of Why*, for the reasons I gave to readers of my book review.

On page 3-5, lines 8-12, the draft PA quotes from EPA's earlier 2011 document as follows:

> An analysis of air quality and population demographic information indicated that the highest $PM_{2.5}$ concentrations in a given area tended to be measured at monitors in locations where the surrounding populations were more likely to live below the poverty line and to include larger percentages of racial and ethnic minorities (U.S. EPA, 2011, p. 2-60).

I have not reviewed the analysis referred to in this passage, but what the passage tells me that there is an association, perhaps a very strong one, between socioeconomic status (SES) and concentration levels of $PM_{2.5}$. Might the "causal relationship" go the other way? Poorer people tend to live in more polluted areas, but it is access to medical care, lifestyle issues such as diet and drugs, and perhaps poorer housing conditions including lack of air conditioning and inadequate heating/insulation, which may cause the increased mortality. I did not find ANY discussion of this important question in the draft PA. A Google search identified multiple studies on SES and mortality, without consideration of PM air pollution as an important causal factor. These studies (Crimmins and Saito, 2001; Adler, 1994; Anderson, 1997; Bosworth, 2018) indicate that SES has a strong association with life expectancy. There is a large

literature from studies on this issue. Why is this literature not addressed in the draft PA – and in other, earlier EPA documents?

The draft PA lists $PM_{2.5}$ has having a "causal" relation to both short-term and long-term mortality in Table 3.1 , page 3-18. Page 3-16, lines 11-13 defines the top of the five EPA categories as:

> Causal relationship: the pollutant has been shown to result in health effects at relevant exposures based on studies encompassing multiple lines of evidence and chance, confounding, and other biases can be ruled out with reasonable confidence.

Maybe I have missed something from the history. I have not read the 2009-11 documents, but what I have read persuades me that confounding via factors associated with SES should be addressed thoroughly in order to satisfy the condition that "confounding and other biases can be ruled out." I have not yet found that EPA has satisfied that condition. That seems to me a very serious flaw in the draft PA.

Let's consider cardiovascular effects disease rather than mortality as the end point. This is listed as causal for $PM_{2.5}$ in Table 3-1, Might there be confounding by socioeconomic status here as well? Again, a Google search leads to a large literature, none of which I have found referenced in the draft PA. A recent example is Schultz, 2018.

I cannot claim to be an expert on this literature on SES and public health. But I can claim some expertise on the analysis techniques, and until I learn more, I do not accept the claim dating back to EPA's 2009-11 documents that a "causal relationship" is clearly demonstrated at and below the level of $PM_{2.5}$ in the present NAAQS. At very high concentrations, I am convinced: People die from smoke inhalation.

Theme II. The concentration response (C-R) relationship. There is a need to address uncertainty and variability and especially at the low concentration levels of the present annual average and 24 hour average $PM_{2.5}$ NAAQS and below. The place for this need to be met is in Chapter 3 and Appendix C.

I am moderately familiar with EPA's BenMAP-EC computer program, having managed the review of papers dealing with it for the journal *Risk Analysis*. The March 2015 issue includes a Smith and Gans paper, a response to it from members of EPA's staff, and a rebuttal from Dr. Smith. In my judgment these three papers present a good introductory discussion of the issues on the limitations of BenMAP-EC for dealing with epistemic uncertainty, such as the shape of the C-R relationship. In September 2016 *Risk Analysis* published a special issue on air pollution risk, which highlighted the need for better characterization of uncertainties, especially on the C-R relationship. I have included these papers in the references at the back of this Response. I managed the peer review of these papers and wrote the introduction to this issue (North, 2016). Contributors included two former chairs of CASAC, Christopher Frey and Roger McClellan, as well as the current chair, Tony Cox. To my surprise and disappointment, I have found NONE of the papers mentioned in this paragraph included in the references for Chapter 3 and Appendix C in the draft PA.

Yes, there is not clear evidence of a threshold for mortality or for cardiovascular (CV) effects. But NEITHER is there clear evidence for linearity at very low concentrations. Most of the data from deaths and CV effects comes at the high dose levels, and a straight line is estimated from these data. (See for example, the acknowledgment of this pattern in Footnote 40, page 3-67.) The procedure EPA is using is an extrapolation from the concentrations at which there are extensive data to levels at which data are

sparse. And by combining data from different areas of the country where $PM_{2.5}$ comes from different sources, data on possible heterogeneity (different slopes in different locations) is being lost.
At the CASAC meeting in 2018, a presentation was made with a follow-up written submission from the Electric Power Research Institute about epidemiological methods to disagggregate spatial variation, with four recent papers describing and applying these techniques. CASAC in its April 11 letter recommended that three of these papers be added in revising the ISA draft. The fourth paper, Eum et al. (2018) was an attachment to EPRI's written submission. I believe methods and applications for spatial disaggregation should be included in the ISA and the PA. The Chapter 3 risk assessments should at least discuss these methods. It would be even better to use the data and results from published applications.

Dr. Anne Smith has written a Perspective paper which has just been accepted for publication in *Risk Analysis* after multiple rounds of peer review and revision. I have communicated with Dr. Smith and received a manuscript copy of the final text and figures. The paper is now being typeset and will appear within a few weeks on the Early View website that provides web access to papers accepted for *Risk Analysis* but not yet published in a print issue. In this paper Dr. Smith proposes a weighting of the C-R relationship below the range with extensive data for a judgment-based estimate of premature deaths avoided by changes in the standard. This weighting is a matter of judgment in the absence of data. It should be recognized that the Administrator must rely on judgment as the basis for his decision because of the sparseness of the data and the uncertainty in the C-R relationship at low concentrations. I urge that Dr. Smith's proposal be considered by CASAC. It seems far better to me than the extensive tables of numbers in Chapter 3 and Appendix C, which, to many readers, might provide an appearance of scientific information and rigor. To me these tables are no better than repeated back-of-the-envelope calculations made with the highly questionable assumption of a linear-through-zero C-R relationship. CASAC has suggested a quantal and graded C-R assumption. A sigmoid shape would seem much more sensible on biological grounds than a linear-to-zero shape. Why assume that many deaths and cardiovascular effects will occur from exposure to concentrations below the present NAAAQS, and below potential new NAAQS at the lower values used in Chapter 3 and Appendix C of the PA draft?

The extreme levels of detail in modeling air quality at the level of a 12 km grid make little sense to me. The mass of detail will confuse readers rather than help them to understand what has been done in the quantitative assessment of risk. I would much prefer a set of regional scenarios, showing how specific sources of PM might change under different standards and strategies for attaining these new standards. That brings me to theme III.

Theme III. Wildfires as a source of PM, especially $PM_{2.5}$.

Chapter 2 presents a summary of the evolving information on sources of particulate matter in the various size classes. It seems to me very important for CASAC members to consider Figures 2-2, 2-3, and 2-4. Fires provide more than half of the national emissions of organic carbon. In urban areas a significant portion of ambient $PM_{2.5}$ and PM_{10} come from mobile sources and stationary fuel combustion, but the organic carbon and elemental carbon portions of PM deserve serious attention as a public health hazard. In the past the attention in the air pollution community was on sulfur oxides and nitrogen oxides, particularly the secondary particulates undergoing long range transport. Figures 2-2 and 2-3 and accompanying text tell that now fires, dust, and agriculture account for the majority of the national emissions – about 2/3 for $PM_{2.5}$ and more than 80% for PM_{10}.

When a large wildfire occurs and the wind blows the smoke into populated areas, the levels of $PM_{2.5}$ go far above the current standards to levels listed by EPA as "unhealthy" and "very unhealthy." I and many

others in the San Francisco Bay Area experienced such levels after the Camp Fire in November 2018. I found a link to my local public television station, whose news coverage included a summary of 24-hour readings at a single monitoring station (Goldberg, KQED, 2018). Shown with this story (you can follow the link in the Reference section) is a set of 24-hour $PM_{2.5}$ readings ranging from 158 to 249, over multiple adjacent days. Compare these big numbers to the 24-hour NAAQS standard of 35. Of the 30 highest readings, 18 were due to two recent wildfires, and 9 others were due to residential wood smoke. Only three of the 30 were from other sources. Similar high concentrations occur, quite frequently, from wildfires in Southern California.

Footnote 21 page 2-21 for Figure 2-7 is one example where wildfire contributions to $PM_{2.5}$ have been removed from a presentation of $PM_{2.5}$ data over time. Has EPA done more of this in its risk assessment? I believe the answer may be yes, and that concerns me. See 2-41, line 23. The text on 2-47 reports that in 2015 the areas with annual mean concentration of $PM_{2.5}$ greater than 11 $\mu g/m^3$ in 2016 are limited to California and southwest Arizona. These are potential annual standard violations with a lowered standard. The text on 2-44, line 10-11 notes that some of the largest difference [among projections from modeling] occurred over southwest Arizona. What source would be causing these high levels? Smoke from fires? Windblown dust, perhaps associated with agriculture? Why are there large differences from different modeling assumptions? When I look at the plots in Chapter 3 for where the annual average and 24-hour NAAQS standard may be exceeded, I see areas in California where smoke is frequently present from large wildfires. In Chapter 3 and Appendix C I find suggestions that rather than focus on the infrequent wildfire events that result in these persistent high levels, far above existing standards and clearly a threat to public health, these episodes are either averaged in, or possibly deleted from the data being used. (See for example, the text on C-16 and 17). I have not taken the time to understand the details, but I would like to understand better the data and the projections by modeling of concentrations used in the risk assessment. Why should California and southwest Arizona be leading candidates for non-compliance under stricter standards?

President Donald Trump tweeted about the cause of California's massive wildfires: "poor forest management" (Pierre-Louis, 2018). As one who has consulted to the US Forest Service on risk management for wildland fires, I am in agreement with the President - after a clarification that many fires occur near the urban-wildland interface on land that would not be readily described as forest, but rather bushy hillsides or even grassland. Congressional law and practices of the U.S. Forest Service and many fire agencies in California and elsewhere in the country have emphasized putting fires out when they occur, rather than managing the fuel – the material that is available to burn. The result of fire exclusion is fuel build-up. Then when a fire gets going under conditions of high heat, high wind and low humidity, the fire is so intense that it is often unstoppable: It burns until the weather changes or it runs out of fuel. Strategies to reduce the risk of large fires are readily available, for example use of grazing animals (Daniels, 2016), mechanical brush and selective tree clearance, and use of prescribed fires under mild weather conditions (Fernandes, 2003). But these strategies come at a cost and someone must provide the funds. EPA and other federal agencies could act to improve this situation, and so benefit public health by reducing the frequency and severity of high PM concentrations from wildfires. CASAC might want to comment on strategies to achieve public health goals by managing wildfires and perhaps other sources of PM, such as from dust and agriculture, shown in the Figures and text of Chapter 2. Evaluating the public health benefits of these strategies to reduce PM from wildfires would be a good addition to Chapter 3. Perhaps other strategies for other sources might be good additions as well. The PA might summarize what states are doing in state implementation plans to reduce emissions from sources such as diesel engines by retiring older vehicles with high emissions. Suggestions might be listed for specific strategies that might be added in the local areas where standards could be exceeded.

Now let me turn to the questions from the CASAC Members.

Questions from Dr. Steven Packham:

I will take your bullets in order.

1. I think biological causation and causality in epidemiology are areas of weakness in the PA draft, and that these weaknesses go back to earlier documents and earlier rounds of CASAC review. I am not qualified to speak on pulmonary toxicology. I hope others can do this.
2. I have provided references that I hope will be helpful. I think the confounding by weather and SES is a most urgent need for further attention. I am surprised and disappointed that relevant recent peer-reviewed publications have not been included in this "last and final" draft PA. While CASAC comments on the ISA are acknowledged in footnotes, references recommended by CASAC have not been included in this draft PA. EPA should have had time to do this.
3. I would like to see more analysis using spatial and source disaggregation. Weather data and SES characteristics of the exposed populations should be collected and used in the analysis of the epidemiological data.
4. Humans have been breathing wood smoke since we learned to use fire millions of years ago. The data on physiological impacts from wood smoke inhalation ought to be extensive.
5. I would also like to see dust separated into natural and anthropogenic sources. I wonder about the high levels in the Salt Lake City area in the figures in Chapter 3. Is this windblown salt from salt flats and from the Great Salt Lake? Case studies in Chapter 3 would be helpful. EPA should be encouraged to separate the sources by type of PM, which is done in Chapter 2 but not in Chapter 3.
6. I have discussed wildfires as an example. If subsidizing landowners to run goats, sheep, or cattle on land that will otherwise grow flammable bushes and trees will reduce the risk of massive fires, EPA ought to be encouraging such strategy. I have been involved on private land in getting a plan for mechanical clearing approved and implemented, as part of timber and fire management under California law and regulation. I'm proud of it. I wish many others would learn and do something similar.

Questions from Dr. James Boylan

Chapter 2. My expertise on PM Air Quality is rather marginal. I learned a good deal from this chapter, and from what I could tell, the material seems scientifically sound. Your questions probe at a depth beyond my knowledge.

Chapter 3 (and 4). I found Chapter 3 and the supporting Appendix C very disappointing. The methods are old and in my judgment, out of date. See my comments on themes I and II above. I will not attest that the material is scientifically sound by current standards. I believe the material is out of date and needs to be redone. The research needs discussion of Chapter 4 seemed sparse and unimaginative. I've provided a few ideas. My favorite would be a serious effort to sort out the contributions of PM, SES and weather variables. I think leading experts in statistics and analyses of big data sets could do it. It would not be for this round on PM NAAQS but perhaps for one five years hence.

Appendix C. In my available time I have not tried to learn about Downscaler and other modifications on the data to "just meet" current and alternative standards. I judge these to be bells and whistles rather than the essence of the needed analysis, which should address confounding, causality, and the uncertainty and variability of the concentration-response relationship for different sources (different chemical species) of PM and in different locations, with different weather and populations with different SES characteristics. I regard BenMAP-CE as far too simple on the C-R portion and far too complex in its adjustments on air quality data. I would like to see case studies on specific areas where the $PM_{2.5}$ standards might be exceeded, such as the areas east of San Francisco and Los Angeles, southwest Arizona, the Salt Lake City area, and selected eastern urban areas. The estimates of mortality with current and alternative standards, based on old studies with the Cox proportional hazard model – that is, linear- to- zero concentration response - are not anything I could endorse or defend.

Questions from Dr. Mark Frampton.

1. For reasons I have discussed under Theme I, I am not persuaded that the 2009 ISA or the 2018 conclusions of a "causal relationship" as EPA has defined this term, are valid. Now that I have found the EPA has found an association between PM levels and SES, I believe that the appropriate action is not to make low SES a sensitive group, but consider that SES has an observed association with PM ambient concentration levels and that this is a potential confounding factor. I don't claim any expertise on the SES and mortality relationship. But it looks to me like there may be an association that might be causal for mortality from other factors, and independent of air pollutant concentration at low levels. Tony Cox's example of association and not causation is whether ice cream sales predict heat stroke. Judea Pearl's example is whether children's shoe sizes predict their reading ability. These are examples of strong association where common sense would say there is no causal relation, that the causal relationship is elsewhere, and what we have is confounding from another factor (temperature; children's age) that is causally related to the end point of interest and the predicting variable.
2. I believe the impact of heterogeneity should be studied. This should give insights on the location and character of the risks that need attention from our national leaders. I think reducing $PM_{2.5}$ from future wildfires is a good candidate activity, based on readily available present information. I believe the level of uncertainty on mortality and other health effects from PM addressed in the PA from exposures at, below, or slightly above the current NAAQS is high. These effects might be essentially negligible as a public health issue – at this point we do not know. But there is no doubt that people died of smoke inhalation in California's recent wildfires, and many more may have suffered health impairment. At the exposures that occurred in California in November 2018, causality seems quite clearly established: People with compromised lung function were asked to wear masks, stay indoors, or leave the area. Members of my family followed these instructions.
3. As you can ascertain from reading my book review, written well before my engagement as a consultant to CASAC, I am a fan of Dr. Cox's concepts of causality determination, although I may disagree with him on details and on how to explain these concepts in simple language. I highly recommend to you reading "The Book of Why" by Judea Pearl. Dr. Cox learned of these concepts from Dr. Pearl's earlier writings, which are much harder to read. For "The Book of Why" Professor Pearl was aided by a good science writer. With my limited available time I am going to skip the 4 documents you listed for comments by the non-member consultants. I did read Dr. Vandenberg's response to Dr. Cox and found it unpersuasive. Dr. Vandenberg seems intent on defending past EPA practices, without going into the issues that were discussed in the

papers in the September 2016 Special Issue of *Risk Analysis*. I will be pleased to read the other three documents and respond on them in a future communication, when there is a sharper focus on specifics, and I have more available time.

4. I see the same confounding issues with SES and weather as applying to cancer as well as mortality and cardiovascular effects. Cancer rates vary in different societies with different diets and other exposure to biologically active substances. I am aware that there is evidence that cooking with some types of coal in enclosed household spaces in China led to an elevated incidence of lung cancer (Seow et al, 2014). Was this lung cancer response from PM or volatile organics released from the coal? Some coals appeared worse than others. In a situation like this with very high exposure levels, I would be strongly inclined to endorse a causal relationship. I would speculate that if people were cooking indoors with wood fuel and with the same lack of ventilation as in these rural Chinese homes, there might be elevated levels of lung cancer.
5. Because of Theme I and Theme II, I do not view the risk assessments of Chapter 3 in this draft PA as either complete or appropriate. These seemed to me a barely warmed-over version of what was done in 2009-11. I believe these risk assessments are superficial and out-of-date. New epidemiological studies are available, and spatial disaggregation might be done and used by EPA. Some references have already been recommended by CASAC to EPA for including in the revised ISA. These should be discussed in the PA as well.
6. I expect there are lots of key studies that ought to be considered in Chapters 3 and 4 of the PA. Other may be better at identifying them than I am, with limited time. I would like to learn more about the data and analysis underlying the quote from EPA 2011 that is at the top of page three of this communication. What is the strength of the observed association between $PM_{2.5}$ exposures and the SES level of the populations receiving these exposures?

Questions from Dr. Sabine Lange:

1. I do not believe I understand EPA's motivation for the "pseudo-design value" adjustments. Your Houston data illustrates that on a day-to-day basis, the data points are highly variable and a seasonal pattern is not evident. I would like to see more attention to patterns of exposure, such as an occasional week-long exposure to levels three times the top value on your figure, which many of us in my part of Northern California experienced in November 2018. Is there a cumulative effect from repeated daily exposures to high levels, on the biological basis that some fraction of $PM_{2.5}$ material inhaled is retained in the lungs? Does toxicity depend on solubility, or on the composition: elemental carbon, organic carbon compounds, oxides of sulfur and nitrogen, etc. I was surprised reading the extent of wood smoke and dust in $PM_{2.5}$ in the west, compared to other constituents. My overall impression is that much more could be learned about the constituents of PM, because there is better data on what is in $PM_{2.5}$ in different locations. There is not uniformity in the national exposure. Yet an averaged-over-the-nation concentration response relationship is used, with the only variation being which epidemiological study is used for the slope coefficient, e.g., the beta value.
2. Again, I do not believe I understand the motivation for these pseudo-design values. It seems to me that a short term effect should show up with screening by lag times. I would be concerned more about high levels that persist over multiple days rather than a single high 24-hour value. Annual averages might be appropriate if effects build up over years of exposure, which I think is the case for inhaled tobacco smoke. But this sort of issue is not in my area of expertise. I was trained as a physicist, and then switched to using training in math and probability for risk analysis. What I know of toxicology comes in large part from a few years of serving on the EPA

Science Advisory Board's Environment Health Committee. I think you ask a very good question - the pattern of exposure should be important. And the toxicity may vary, depending on chemical composition as well as particle size and exposure pattern.

3. If long-term exposure underlies the health response, then whether subjects move in and out of the area is important. I learned this from cancer epidemiology. Again, I would like to see case studies on specific areas. The greater Salt Lake City area shows up green in the Chapter 3 - Figure C-17, page C-18. Green represents exceedance of the 24 hour standard. What is going on here? Is this from wind-blown salt/grit off of the Bonneville Salt Flats or the Great Salt Lake? I doubt it is from fires and dust, as in California and Oregon. The draft PA text does not help me at all to understand what is going on. I found a local news story (Jacobs, 2016) that indicates lowered levels from evaporation from the Great Salt Lake are creating an extensive dry area with a salty "crust," and resuspension of materials from this crust may be adding to the level of dust, including toxic materials from industrial sources deposited in earlier times. Such local stories suggest that trying to regulate based on national standards may miss locally important air quality problems. EPA ought to be more sensitive to this, and evaluate regulatory strategies that fit the local problems.
4. I respond with an emphatic yes to your question. There are lots of possibilities. For example, see the Anne Smith paper of March 2015 and her newly accepted paper.
5. Another emphatic yes. By combining the C-R relations from different areas the effect of the speciated constituents will be masked. Don't mix Salt Lake salt and old deposits of trace metals resuspended by wind from the evaporated portions of the Lake, and California's wood smoke exposures. Get information on each separately!
6. You ask great questions! Yes, if you mix it all together then you can't tell which ingredients in the resulting stew may be toxic. C-R ought to be done with disaggregation, so one can see the effect of speciation. And it may be that weather and SES are even more important than PM of any species at low levels in predicting health effects. Let's include these factors separately while gathering the data. By separating them we might develop much better information about the impacts on public health, and what strategies might reduce adverse impacts on public health.

Questions from Dr. Tony Cox

1. I don't believe the C-R coefficients are conceptually very useful, because of what I have described under themes I and II. These coefficients may be well-defined in terms of the Cox proportional hazard model from the listed epidemiological studies. But given the adjustments on the concentration side, the potential extent of confounding by weather and SES, and the uncertainty in response at low concentrations, I could not defend the calculations of these betas as a proper basis for setting NAAQS.
2. I would chose a, association, over b,c, and d. I have trouble imaging what intervention means for the aggregated PM concentration across the entire nation. Maybe e is the best answer, something different than any of the above. I am puzzled by why EPA chose spatial aggregation rather than trying to learn from disaggregated C-R data where available.
3. My theme I is evidence of potential confounding from SES and possibly weather variables as well. I can't attest to more than slopes of regression lines (association) from the epidemiological data. The basis is association, not a causal relationship that I can endorse.
4. As a follow-on to the previous question, I do not believe that a causal relationship has been established for any of the endpoints in Chapter 3, Table 3-1.

5. I'm not sure I can judge what is "generally accepted." I can judge what I think is acceptable and believe should be generally accepted. I believe that the strong association implies causality aspect of the Bradford Hill Criteria is out-of-date and should no longer be used. But the Bradford Hill Criteria may still be "generally accepted" by many epidemiologists and public health experts. Scientific revolutions happen slowly, according to Thomas Kuhn's book.
6. The problem with $\Delta y/\Delta x$ is that there may be multiple factors $x_1 \ldots x_n$ that affect y. Why should the other factors be excluded when there is evidence that these other factors may be important influences on y? A one-dimensional regression analysis of health effects on one air pollution concentration doesn't seem like a definitive basis for prediction. Your example is a good one. Temperature should be included in the analysis. Changes in ice cream consumption may have had a strong association with heat stroke – certainly in my youth, before the widespread availability of air conditioning. I remember as a kid waiting eagerly for the arrival of the Good Humor Man on hot summer days.
7. If there is any empirical validation of the beta coefficients, which would support approximately accurate predictions or simulations on how air pollution interventions would change population health responses, I have missed it in my reading of the draft PA. I think such estimates could be developed with spatially disaggregated data. If SES and weather variables were included, this analysis might be very instructive on the potential result of such interventions. I recall you have such an example in your *Causal Analytics* book. I would strongly advocate to EPA trying this type of analysis on regional problems, based on larger data sets than may be currently available.
8. I did not find more than a few dismissive words about "potential omitted confounders" in Chapter 3 and Appendix C. The absence of discussion on SES and weather was disappointing. An at Dr. Frampton's urging I read the response letter to you from Dr. Vandenberg. I thought he was defending old EPA practices with little indication that EPA is open to new ideas. And I am appalled that there are no references in the draft IPA to the many relevant papers published in the past few years in *Risk Analysis*.
9. If there was much sensitivity analysis beside which location and which (old) epidemiological study, I missed it.
10. Model uncertainty on the C-R relationship was not adequately discussed or included.
11. Yes, the discussion of exposure estimation uncertainties and estimation errors was also inadequate.
12. Themes I, II and III motivate me to withhold any endorsement that the draft PA provides an adequate basis for assessing causal impacts on public health of changing $PM_{2.5}$ levels. And I do not understand, nor do I believe the public will understand, the complex and convoluted way that EPA describes changes in concentration with alternative standards. What sources of $PM_{2.5}$, as described in Chapter 2, will be reduced, and by what amounts?
13. Your question addresses my Theme I concerns. I did not find these addressed in the draft PA.
14. My response is a strong NO.
15. I think that CASAC should be advising EPA on how to do a better analysis. It may not be possible to get such analysis done by the time of finalization of the PA. But EPA should at least include discussions of new epidemiological methods and recent studies with spatial disaggregation, such as those discussed in the Comments submitted by EPRI at the last CASAC meeting.
16. I am pessimistic that that the techniques of formal causal modeling can be incorporated in the final version of the PA. Maybe Chapter 4 can be expanded into a research plan that describes these methods and lays out steps toward using them in future PM reviews. Developing the detail you ask for is far more than I can describe in the very limited time I have to write these comments. (It took me a good deal more time to read and review your *Causal Analytics* book,

which touches on many of these details.) The hardest aspect may be in collecting the needed disaggregated data – on sources, concentrations, health endpoints, SES factors, and weather factors. I would recommend some regional or local case studies to EPA before trying to do a national analysis that includes such disaggregated data.

I'll add a summary statement of my own. I think the Administrator may be given relatively little useful new information on the impact of changing the Primary PM standards from what has been assembled in Chapters 3 and 4 of this draft PA. (I have not read the supporting material on Secondary PM standards.) If CASAC should agree with me, then that judgment needs to be explained to the Administrator. Perhaps a new and much simpler analysis, such as in Anne Smith's Perspective piece, might be used in a greatly revised final PA, with uncertainties and sensitivity analysis highlighted. I am not persuaded that a case has yet been made for stricter national standards, but I believe that more aggressive strategies to control sources may be needed in certain locations, such as wildfire-prone areas in California and areas affected by wind-blown PM from land once covered by the Great Salt Lake. There may be other important candidates for additional study of source control strategies.

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