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Comments on EPA's Integrated Science Assessment (ISA) for Particulate Matter (External Review Draft – October 2018)

By

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I appreciate the opportunity to offer brief comments to the Clean Air Scientific Advisory Committee (CASAC) on the draft document, "Integrated Science Assessment (ISA) for Particulate Matter." This important document reviews the science that under-girds the policy decisions that must be made by the EPA Administrator in either reaffirming or revising the National Ambient Air Quality Standards (NAAQS) for Particulate Matter (PM).

The comments I offer are grounded in my more than 40 years of service on EPA Advisory Committees concerned with setting air quality standards. That service began in 1977 when I chaired an *ad hoc* committee to review the Criteria Document that was the scientific basis of the first NAAQS for lead. The positive impact of that advisory committee was one factor encouraging amendments to the Clean Air Act that led to the establishment of what is now called the Clean Air Scientific Advisory Committee (CASAC). I would later serve on the first CASAC to review the science on PM and ultimately, over the decades, participate in CASAC panels that considered the science under-girding all of the NAAQS indicators. In 1988-1992, I had the honor of serving as Chair of CASAC. For more than 50 years, my primary professional goals have been focused on creating an improved scientific knowledge base on the health effects of airborne materials, information essential for decisions that will improve the quality of human lives.

The NAAQS setting process was initially grounded in Criteria Documents and, more recently, ISA's that are intended to document, integrate and synthesize the scientific information that will under-gird the policy decisions that must be made by the EPA Administrator in either reaffirming or revising each NAAQS. The quality of these documents is critical to the quality of the science policy decisions that are made by the EPA Administrator.

With my background it should not be a surprise that my comments will have a strong historical orientation. I was born in Minnesota and grew up in the State of Washington so I have experienced superb air quality. However, even in those pristine environments I recognized that human activity could impact air quality. In 1944-1945, I lived in Richland, WA adjacent to the Hanford Nuclear Site. There I experienced high velocity winds from the southwest which carried soil dust of volcanic origin at concentrations that would reduce visibility and impact human health. These winds were called "termination winds" because after the winds subsided employees lined up at the Personnel Office to terminate employment and head home to more pleasant environments. As a youth, I also experienced driving by pulp mills whose emissions

would burn one's eyes and throats. As a teenager in the 1950s, I visited areas in the industrialized east and in southern California with terrible air quality. I also remember, as a youth accompanying my grandparents to funerals of old-timers, in those days individuals who lived for 60-70 years were considered old-timers.

Today, the situation is remarkably different. In my opinion, this relates in part to the Clean Air Act of 1970 and subsequent amendments that provided EPA the legislative authority to take actions that have substantially improved air quality. Society-at-large has responded. Major technological improvements have been made in many sectors, including electrical power generation, transportation, and manufacturing. These have yielded substantial reductions in emissions along with increased productivity. There have also been substantial improvements in the quality of life and disease prevention such that Americans, on average, have never lived longer. As an aside, there have recently been troubling indicators that life expectancy is being shortened by the opioid health crisis and suicides. America is also challenged by differences in socio-economic status impacting on life expectancy.

I provide this general background because what I have succinctly described is lost in the encyclopedic nature of the current draft ISA. This is a critical deficiency since the Administrator in making decisions on the reaffirmation or revision of the NAAQS PM must consider the science in a broad societal context. The current draft ISA does not provide the EPA Administrator with the context on improved air quality and health of Americans required to make critical judgments on "how low is low enough" in selecting concentrations and statistical forms for each PM indicator and averaging time.

I am compelled to suggest that the Agency is using the science/policy/regulation paradigm developed four decades ago to reaffirm or revise NAAQS today. The situation today has changed remarkably from those earlier decades. The air is substantially cleaner, improved technologies have been developed, population morbidity and mortality patterns have changed and differences in air quality across the USA are more apparent than a half century ago.

Advisory Role Not Standard Setting

As a prelude to my comments I wish to emphasize that the role of the CASAC is to provide advice to the EPA Administrator that will aid the Administrator in making the policy decisions that determine the four elements of each NAAQS indicator, averaging time concentration and statistical forum. The Committee's role is not to set the NAAQS; that is the

responsibility of the Administrator. Nor should the CASAC frame its advice in such a narrow manner that its advice dictates a specific level. The CASAC needs to be mindful that there are no scientific algorithms that translate a large body of knowledge into specific NAAQS. The crucial decisions on "how low is low enough" are policy judgments informed by scientific knowledge. I have addressed these issues in a paper entitled, "Role of Science and Judgment in Setting National Ambient Air Quality Standards: How Low is Low Enough?" (McClellan, 2012).

Lack of Context

A key deficiency in the current draft document is a lack of context for the current review of the PM NAAQS. I addressed the issue of context in a recent publication entitled, "Providing Context for Ambient Particulate Matter and Estimates of Attributable Mortality" (McClellan, 2016). Figure 1, from that paper, uses $PM_{2.5}$ levels from the Harvard Six Cities Study to illustrate the substantial reductions in $PM_{2.5}$ that have occurred in all six cities in that classic study from the mid-1970s through 2009. Figure 2 illustrates the substantial reduction in death rates for the U.S. population from 1960 to 2010. Not only has the death rate been reduced, there have been important shifts in the causes of death (Table 1). The information presented in Tables 2 and 3 help provide perspective on estimated excess or premature deaths attributable to PM exposure.

As one considers epidemiological findings on chronic diseases, such as Chronic Obstructive Pulmonary Diseases and Ischemic Heart Disease, it is important to recognize that deaths observed, for example in 2000, may be traceable to exposures and other circumstances that occurred decades ago. By the same token it is my view that we have not yet experienced all the positive health benefits of the improvements in air quality experienced in most parts of the USA over the last several decades. We are on the right trajectory for further improvements under the existing standards.

This information is important because epidemiological studies are typically grounded in estimation of the impact of various factors such as past PM exposure on the relative risk for various health endpoints. Baseline rates are important to provide perspective for calculation of excess risk attributable to a factor such as air quality. With improvements in air quality, estimates of excess risk attributable to air pollution in recent studies are very small and frequently not statistically significant. In short, the role of air quality as an influencing factor on

population health in 2018 is substantially different than was the case when the Clean Air Act was enacted nearly a half century ago.

Beyond the need for historical context, there is a need for the ISA to provide perspective on the role of other factors that impact human health. One of the most important of these factors is Socio-Economic Status as illustrated in Table 4. The calculated impact of Socio-Economic status is substantial unlike the estimates for PM and other air quality indicators that blend into the background. As an aside, I am concerned that many epidemiological studies of air quality have not adequately considered Socio-Economic Status as a variable.

Lack of Conceptual Base

In many sections the draft ISA does not provide a clear conceptual basis for the details presented in encyclopedic fashion. This is especially true of the sections dealing with health effects. The detailed science needs a better conceptual framework. I will cite several major conceptual issues.

One deals with the use of absolute versus relative risk models for analyzing and interpreting exposure-response relationships. Relative risk models are widely used in the conduct and interpretation of epidemiological studies. This is highly appropriate when attempting to "tease out" the effects of one putative risk factor, such as air quality, from a myriad of factors influencing the health outcomes being investigated. The obvious needs to be stated – "poor air quality does not cause any unique diseases." The disease conditions of concern have many etiological factors and most likely are multi-factorial in their etiology.

In contrast, scientists conducting studies with cells, tissues and whole animals typically use absolute exposure-risk models. Most often, the experimental design focuses on a single variable such as a single air pollutant, i.e. $PM_{2.5}$. Moreover, many of the experimental studies are of limited value because they use only a single exposure level and a few observation times. It is important that the authors of the ISA appreciate that specific mechanisms of action are frequently exposure level related. In short, mechanisms have exposure-response relationships that may change with exposure duration just as the ultimate health endpoint of concern have complex exposure-response reltaionships.

In my opinion, the ISA fails to provide a conceptual basis for bridging between scientific findings obtained with the two types of exposure-response models, relative versus absolute risk. This deficiency complicates the various characterizations of "causality" that are at the core of the

ISA's health assessments. This leads to the nonsensical synthesis statement (pg 1-1) – "Many $PM_{2.5}$ components and sources are associated with many health effects, and the evidence does not indicate that any one source or component is more strongly related with health effects than $PM_{2.5}$ mass." This statement is not factual and is misleading!

Association Does Not Equal Causality

In my opinion, the discussion of the role of the epidemiological studies in evaluation of "causality" for specific health endpoints is seriously flawed. In the ISA, there are repeated attempts to equate statistical associations with evidence of causality. This important topic has been addressed in research papers by Louis Anthony (Tony) Cox**, "**Modernizing the Bradford Hill Criteria for Assessing Causal Relationships in Observational Data" (Cox, 2018) and "Do Causal Concentration–Response functions exist? A Critical Review of Associational and Causal Relations between Fine Particulate Matter and Mortality" (Cox, 2017)

The concept of "causality" used in the ISA appears to be based in large part on traditional approaches in toxicology and medicine that dealt with single etiological agents and well-defined disease outcomes. The use of simplistic single pathway models was useful in helping advance science. However, advances over the last decade have shown that specific kinds of cancer and other diseases of concern for PM likely arise from a multiple etiological factors operation via a network of mechanistic pathways leading to disease. How these networks operate as the intensity and duration of exposure to various risk factors, including various $PM_{2.5}$ components, other air pollutants and other factors is not yet known.

In my opinion, the authors of the ISA misuse the "Causality Categorization" scheme. It is quite clear that exposure to various PM components at sufficient concentrations and durations of exposure are associated with, and, indeed, in some cases, may cause an increase in the excess relative risk for certain disease conditions. This has been known for decades. The ISA, in some sections, seems to have a goal of increasing the number and kind of disease conditions associated with PM exposure. The real focus of the ISA should be on exposure conditions (component, concentration and duration) that are or not influencing the occurrence of diseases at or around the level of the current NAAQS.

Need for Succinct Executive Summary

The most serious deficiency in the current draft ISA is the lack of a succinct executive summary written such that it is understandable by a well-educated lay person. A well-written

Executive Summary, a few thousand words in length, is required to inform Administrators reaffirmation or revision of the PM NAAQS for various indicators. The material presented on page 1-1- "Overall Conclusions of the Particulate Matter (PM) Integrated Science Assessment (ISA)" misses the mark.

I appreciate the opportunity to present these comments as a private citizen. These comments were prepared on my own time and at my own expense. The views expressed are my personal professional views and not necessarily those of any past public or private clients.

I look forward to hearing the presentations and robust discussion at this meeting and to reviewing the written comments of the CASAC members and other public commenters.

I reserve the right to extend and/or revise my comments at a later date.

References

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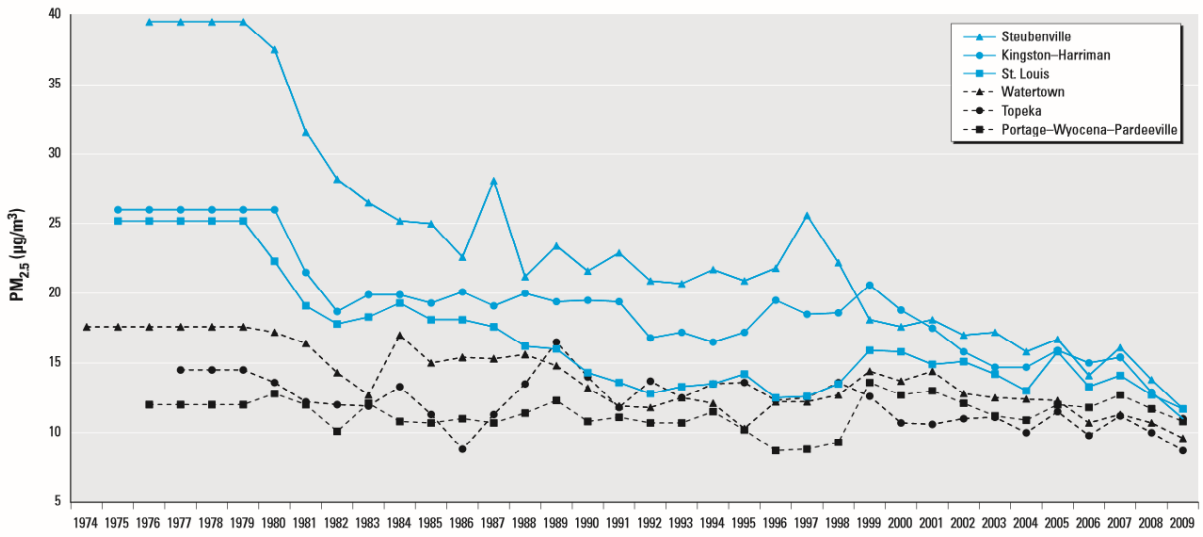

Figure 1 Annual mean $PM_{2.5}$ levels during 1974-2009 in the Harvard Six Cities study (Adapted from Lepeule et al (2012). The data points pre-1997 for $PM_{2.5}$ have been extrapolated from TSP and PM_{10} measurements.

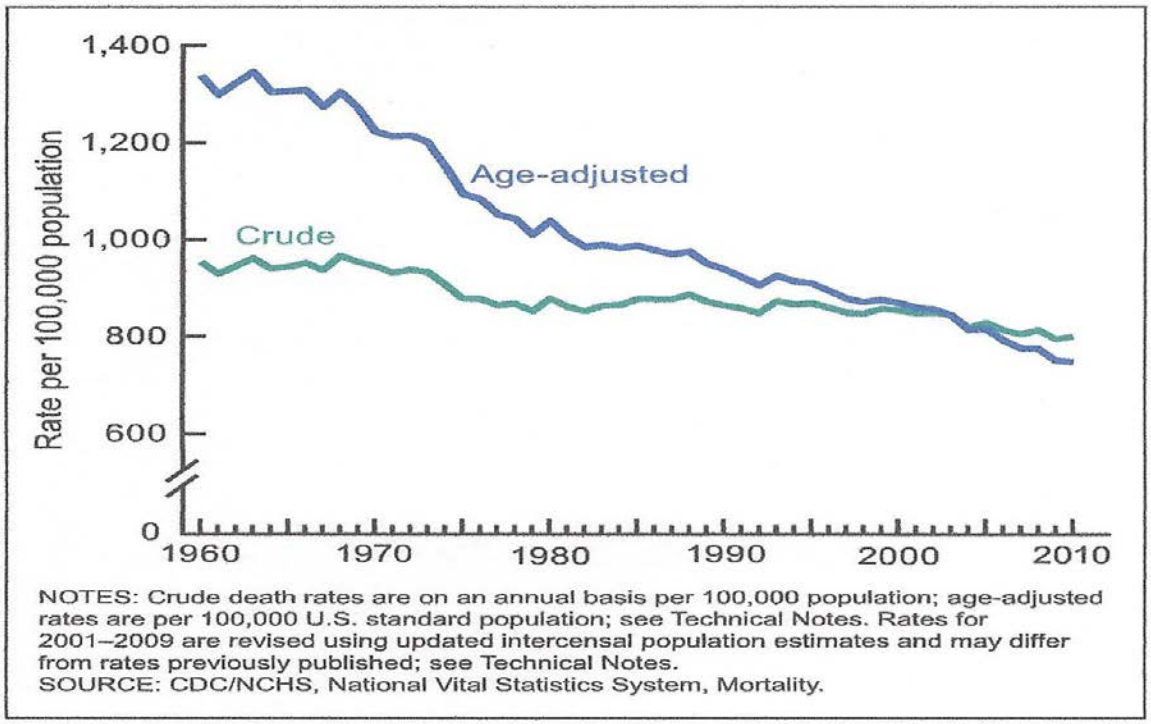

Figure 2. Crude and age-adjusted death rates: United States, 1960-2010 (Adapted from Murphy et al, 2013).

Table 1. Causes of Death for USA for 2010 by Cause (Murphy et al, 2013)

Rank	Cause of Death (based on ICD-10, 2004)	Number
…	All causes	2,468,435
1	Diseases of heart	597,689
2	Malignant neoplasms	574,743
3	Chronic lower respiratory diseases	138,080
4	Cerebrovascular diseases	129,476
5	Accidents (unintentional injuries)	120,859
6	Alzheimer's disease	83,494
7	Diabetes mellitus	69,071
8	Nephritis, nephrotic syndrome and nephrosis	50,476
9	Influenza and pneumonia	50,097
10	Intentional self-harm (suicide)	38,364
11	Septicemia	34,812
12	Chronic liver disease and cirrhosis	31,903
13	Essential hypertension and hypertensive renal disease	26,634
14	Parkinson's disease	22,032
15	Pneumonitis due to solids and liquids	17,011
…	All other causes	483,694

Table 2. Comparison of 2014 Estimated Premature Deaths Avoided Using Alternative Ambient $PM_{2.5}$ Concentration-Response Functions (Adapted from Fann et al (2016 and personal communication , N Fann 2016)

Source of Function	Baseline Mortality (Deaths)	Estimated Premature Deaths Avoided (Deaths 95% Confidence Interval)
Harvard Six Cities Lepeule et al (2012)	2,565,169*	10,373 (6,010, 14,698)
ACS Krewski et al (2009)	2,565,169*	4,582 (3,334, 5821)
Pooled Experts	2,565169*	8,327 (1,492, 18,289)
Meta-Analysis (Beyond 2006)	2,565,169*	5,852 (2,527, 9,150)
Meta-Analysis (Through 2006)	2,565,169*	5,530 (3,287, 7,756)
Integrated Exposure Response	364,408**	3,931 (1,935, 4,241)

*All-cause; **Ischemic Heart Disease

Table 3. Estimates of Avoided Premature Deaths in California in 2020 Estimated for $PM_{2.5}$ NAAQS with a Reduction in the Annual Standard from 15 to 12 μg/m^3 projected using BenMAP (A Smith, personal communication, 2016).

	Population		Baseline Mortality (#)		Avoided Deaths (#)	
	Krewski[a] (30-99)	Lepeule[b] (25-99)	Krewski (30-99)	Lepeule (25-99)	Krewski (30-99)	Lepeule (25-99)
Not attaining/above margin (>13 μg/m^3)	763,104	875,086	7,574	7,681	21	47
Not attaining/in margin (>12 to 13 μg/m^3)	3,841,464	4,419,703	41,853	42,342	117	266
Already attaining (≤12 μg/m^3)	7,560,163	8,537,984	86,913	87,735	318	721
Total	12,164,732	13,832,773	136,340	137,758	456	1,034

[a] Krewski et al (2009) evaluates the population from age 30 to 99 years;
[b] Lepeule et al (2012) evaluates the population from age 25 to 99 years.

Table 4. The Impact of Socio-Economic Status on Mortality Rate Ratio[a] (adapted from Steenland et al, 2004)

Mortality	Men	Women
All causes	2.02 (1.95-209)[b]	1.29 (1.25-1.32)
Heart Disease	1.88 (1.83-193)	1.84 (1.76-1.93)
Stroke	2.25 (2.14-2.37	1.53 (1.44-162)
Diabetes	2.19 (2.07-2.32)	1.85 (1.72-2.00)
COPD	3.59 (3.35-3.83)	2.09 (1.91-230)
Lung Cancer	2.15 (2.07-2.23)	1.31 (1.25-1.39)
Breast Cancer	-	0.76 (0.73-0.79)
Colorectal Cancer	1.21 (1.16-1.27)	0.91 (0.86-0.96)
External Causes	2.67 (2.58-2.78)	1.41 (1.35-1.48)

[a] Mortality rate ratio = $\frac{\text{Mortality for lowest quartile of socioeconomic status}}{\text{Mortality for highest quartile of socioeconomic status}}$
[b] 95% Confidence Interval