

# Comments on EPA's "Integrated Science Assessment for Particulate Matter (External Review Draft)"

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Gradient

Thank you for the opportunity to speak today regarding the Integrated Science Assessment (ISA) for Particulate Matter (PM) (External Review Draft). I am an epidemiologist and board-certified toxicologist at Gradient, an environmental consulting firm. I am speaking on behalf of Gradient, but my time spent preparing these comments and attending this meeting has been funded by the American Petroleum Institute.

CASAC should recommend that EPA address three overarching issues in the draft ISA that undermine its evaluations of health effects. These relate to the systematic review protocol, study quality and relevance, and the causality framework. Specifically, CASAC should recommend that the ISA:

- Include a sufficiently detailed systematic review protocol;
- Sufficiently address study quality by providing detailed study quality criteria, tabulating study quality characteristics for individual studies, and specifying how individual study quality impacts evidence integration;
- Explicitly state study relevance criteria; and
- Update the causal framework in such a way that does not inherently bias towards a causal conclusion.

CASAC should recommend that EPA re-evaluate causality once these overarching issues with the evaluation process are addressed. I understand that re-evaluating all endpoints may not be feasible, but EPA should at least re-evaluate the associations for which causal conclusions in the current draft ISA differ from those in the 2009 ISA. These include long-term fine particulate matter (PM<sub>2.5</sub>) exposure and nervous system effects and cancer, and long-term ultrafine particle (UFP) exposure and nervous system effects.

The current lack of a thorough, systematic study quality evaluation is a serious issue for determining causation, and it is even more problematic in the context of concentration-response relationships. This is because for causal determinations, studies need to establish the presence of an effect; however, for concentration-response relationships, studies also need to calculate the magnitude of an effect in relation to the level of exposure. CASAC should also recommend that the draft ISA conduct a thorough, systematic quality evaluation of studies of concentration-response relationships between PM exposures and mortality, and fully consider the impact of potential biases and uncertainties on the study results.

I have gone into more detail in my written comments, but I wanted to present at least one table here that shows how study quality can be addressed in a systematic fashion. Briefly, studies are in columns, and study quality aspects are shown in rows. Red shading indicates the potential for bias or the presence of uncertainty but does not reflect the magnitude of such a bias or uncertainty on study results. The quality criteria are described in detail in text, as is their impact on the interpretation of results. This is then

considered when integrating evidence and either making causal conclusions or evaluating concentration-response relationships.

These recommendations will allow EPA to evaluate and integrate the evidence in a transparent, systematic, and unbiased manner. As a result, the causal determinations for health effects will not be inherently biased towards causation, and undue confidence will not be placed in observational concentration-response data that have substantial uncertainties.

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## Overarching Issues with the Draft ISA

- Lacks a sufficiently detailed systematic review protocol
- Does not sufficiently address study quality
- Lacks explicit study relevance criteria
- Uses a causal framework biased towards causality

*CASAC should recommend that EPA re-evaluate causality and concentration-response once these issues are addressed.*

## Causal Determinations and Concentration-Response Evaluations Should be Re-evaluated

Long-term Exposure	Outcome	2009 ISA	2018 Draft ISA
PM <sub>2.5</sub>	Neurological effects	Not evaluated	Likely causal
PM <sub>2.5</sub>	Cancer	Suggestive	Likely causal
UFP	Neurological effects	Not evaluated	Likely Causal

*Concentration-response – shape of the curve and magnitude of effect are impacted by bias and uncertainty*

# Study Quality Characteristics Table – Long-term PM<sub>2.5</sub> Exposure and Total Mortality

Sources of Bias and Uncertainty		Crouse et al. (2012)	Crouse et al. (2015)	Villeneuve et al. (2015)	Chen et al. (2016)	Pinault et al. (2016)	Wong et al. (2015)	Beelen et al. (2014)	Cesaroni et al. (2013)	Lepeule et al. (2012)	Hart et al. (2015)	Shi et al. (2016)	Thurston et al. (2016)	Di et al. (2017a)
PM <sub>2.5</sub> Exposure Assessment	Central site monitoring (low spatial resolution)									X				
	No validation for PM <sub>2.5</sub> data						X						X	
	Temporal variation not accounted for	X	X	X	X			X	X					
	Residential mobility not accounted for	X		X		X	X	X		X		X		
	No evaluation on multiple exposure windows	X	X	X	X	X	X	X	X		X	X	X	X
	Personal activities not accounted for (e.g., time spent indoors)	X	X	X	X	X	X	X	X	X	X	X	X	X
Mismatch of PM <sub>2.5</sub> exposure window and mortality	X	X	X	X		X	X	X					X	
Individual Covariates	No adjustment of individual covariates													
	Information bias (e.g., self-reported covariates)	X	X	X		X	X	X		X	X	X	X	
	Temporal variation not accounted for	X	X	X	X	X	X	X	X	X			X	
	Unmeasured confounding (e.g., pre-existing conditions)	X	X	X	X	X	X	X	X	X	X	X	X	X
Ecological Covariates	No adjustment of ecological covariates													
	Temporal variation not accounted for	X		X	X	X	X	X	X	X	X	X	X	
	Residential mobility not accounted for	X		X		X	X	X				X		
	Unmeasured confounding (e.g., access to health care, violence)	X	X	X	X	X	X	X	X	X	X	X	X	X
Evaluation of Copollutants	No adjustment of copollutants													
	Central site monitoring (low spatial resolution)												X	
	No validation for copollutants data												X	
	Temporal variation not accounted for	X	X	X	X	X	X	X		X	X	X	X	
	Residential mobility not accounted for							X					X	
	Personal activities not accounted for (e.g., time spent indoors)		X					X	X				X	X
	Collinearity/nonlinear relationship with PM <sub>2.5</sub> not addressed/accounted for												X	
	Mismatch of copollutants window and mortality		X					X	X				X	X
Statistical Analyses	Model assumptions not tested/relaxed		X	X		X	X	X	X		X	X	X	X
	C-R curves sensitive to <i>df</i> (natural splines)	X	X	X	X	NR	X	X	X				X	
	Nonlinearity not assessed statistically			X		X					X	X	X	X
	Threshold not assessed	X	X		X		X		X	X	X	X	X	X

## CASAC Should Recommend that the Final ISA:

- Include a sufficiently detailed systematic review protocol
- Sufficiently address study quality
- Explicitly state study relevance criteria
- Update the causal framework in such a way that does not bias towards a causal conclusion
- Re-evaluate the health effects and welfare effects
- Re-evaluate concentration-response