American Lung Association.

August 15, 2023

The Honorable Michael Regan, Administrator
U.S. Environmental Protection Agency
William J. Clinton Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Re: Comment on EPA's Guidelines for Cumulative Risk Assessment Planning and Problem Formulation (Draft for Public Comment); Docket Number: EPA-HQ-ORD-2013-0292[1]

The American Lung Association offers the following comments to EPA on its "Guidelines for Cumulative Risk Assessment Planning and Problem Formulation" with specific input on their application in the determination of the primary National Ambient Air Quality Standards (NAAQS) for criteria air pollutants (CAPs).

Ambient air has multiple pollutants, including CAPs like ozone, NO_2, SO_2, and $PM_{2.5}$, which do not exist in isolation, nor are they inhaled individually. Short-term and/or long-term exposures to these CAPs cause or are associated with similar and sometimes overlapping adverse health endpoints. Additionally, climate change imposes a penalty on these conventional pollutants by increasing their concentrations and/or exacerbating their health impacts. Other non-chemical and non-pollutant factors including sociodemographic and socioeconomic elements (*e.g.* race/ethnicity, education level, income, profession, location, age, existing morbidities) also influence the causation, increased risk of development, or exacerbation (*i.e.* exposure-response modifiers) of CAP exposure-associated specific adverse health endpoints.

This is the basic premise of our consistent ask of EPA to consider cumulative impacts (*i.e.* impacts from "totality of exposures to combinations of chemical and non-chemical stressors and their effects on health, well-being, and quality of life outcomes"[2]) in determining NAAQS, including in the current reconsideration of the ozone NAAQS and in the recently initiated review of the NO_2 NAAQS.[3]

In her analysis of what EPA considers in setting primary NAAQS, law professor Deborah Behles observed more than a decade ago: "EPA has designated six pollutants, which all have relationships with each other, as criteria pollutants…. Of these, particulate matter, ozone, nitrogen dioxide, and sulfur dioxide are closely related to each other due to their chemical and

[1] Environmental Protection Agency Risk Assessment Forum. (May, 2023). Guidelines for Cumulative Risk Assessment Planning and Problem Formulation (Draft for Public Comment); Document #: 2023-12972. Note: We appreciate that the CRA Guidelines document clearly lays out the various aspects to be considered and has a navigable table of contents, internal bookmarks and tables of figures and tables, all of which make it easy to peruse the document.
[2] EPA's Guidelines for Cumulative Risk Assessment (May, 2023). GLOSSARY OF KEY TERMS; page v
[3] American Lung Association (ALA). (4/14/2023). Comment on Ozone NAAQS PA Draft 2; ALA – health organization coalition. (2/9/2023). Comment on NO2 NAAQS RFI;

physical attributes, the similarity of their emission sources, and their association with similar adverse health impacts."[4]

Extending this observation to the NAAQS review/revision process, she noted: "Inhaling air pollutants can lead to a variety of adverse respiratory and cardiovascular health effects. This potential risk for health impacts is likely greater when the mixture of pollutants that exists in ambient air, rather than isolated pollutants, are inhaled. Despite the evidence of potential cumulative impacts, EPA has continued to focus its analysis of health impacts on isolated pollutants instead of the actual mixture we breathe…. EPA should evaluate and consider cumulative health impacts when it sets national ambient air quality standards under the Clean Air Act…. Consideration of cumulative health impacts is consistent with the Act's requirement to set standards at a level requisite to protect public health, could translate into a more accurate way to estimate risks, and could provide a tool for prioritization of emission reductions in the most heavily impacted communities."[5]

Research funded by EPA's National Center for Environmental Research also attests to the importance of cumulative impacts in risk assessments of individual pollutants. "(T)o arrive at a realistic assessment of exposure risks, regulatory authorities arguably should consider cumulative stressors and exposure data derived from cumulative risk assessment."[6] Adoption of a multi-pollutant framework that includes "measurements of a rich array of air pollutants, and application and development of statistical methods that are suitable for a large and highly correlated number of variables and that can incorporate what is already known about their interrelationships" will result in "an air quality management program that protects public health through a better understanding of the features of a complex air pollution mixture that are most deleterious to health."[7]

In its Cumulative Risk Assessment (CRA) Guidelines, EPA notes: "CRAs have been performed to inform decisions on some of the National Ambient Air Quality Standards (NAAQS). The NAAQS, as standards for ambient air, reflect consideration of the cumulative concentrations of various pollutants in ambient air, which result from emissions from many sources."[8] But this is only partly true. In setting *primary* (*human health-based)* NAAQS, EPA considers the cumulative risks (in Health Risk and Exposure Assessments) of CAPs *only* among chemically or physically related groups (for which individual NAAQS are set) but not across the different CAPs.[9] The ozone NAAQS, for example, use O_3 as the indicator for ozone and other photochemical oxidants (collectively referred to as Ox), some of which are species with poorly defined properties and more difficult to quantitatively measure but may play a role in ambient health effects, co-occurring with ozone in ambient air.[10] Similarly, NO_2 and SO_2 serve as indicators of multiple nitrogen oxides and sulfur oxides respectively.

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[4] Behles, D. N. (2010). Examining the Air We Breathe: EPA Should Evaluate Cumulative Impacts When It Promulgates National Ambient Air Quality Standards. *28 Pace Envtl. L. Rev. 200,* pages 8-9 (7-8)
[5] *Ibid*. Behles, D. N. (2010). *28 Pace Envtl. L. Rev. 200*, page 2 (1)
[6] Alves *et al*. (2012). EPA authority to use cumulative risk assessments in environmental decision-making. page 1
[7] Vedal, S. & Kaufman, J. D. (2011). What Does Multi-Pollutant Air Pollution Research Mean? *American Journal of Respiratory and Critical Care Medicine*, *183*(1), 4-6.
[8] EPA's Guidelines for Cumulative Risk Assessment (May, 2023). Appendix A-6
[9] EPA. (Aug, 2014). Health Risk and Exposure Assessment for Ozone - Final Report; EPA-452/R-14-004a; This REA for ozone NAAQS is an example of EPA's REA that does not include cumulative risks.
[10] Clean Air Scientific Advisory Committee (CASAC). (11/22/2022). Review of the EPA's Integrated Science Assessment (ISA) for Ozone and Related Photochemical Oxidants (Final Report); EPA-CASAC-23-001; George A. Allen comment, pages 31-33

For the *secondary* (*human welfare-based)* NAAQS, however, EPA considers these CAPs together as co-pollutants: "Cumulative ecological risk assessment has also been performed to inform NAAQS decisions, e.g., in assessing ecological risk associated with the co-occurrence in ambient air of multiple oxides of sulfur and nitrogen."[11] The $PM_{2.5}$ and PM_{10} standards are set for groups of similar sized particulate aerosols: "In the case of risk assessments for fine particulate matter, the assessment is of the whole mixture of fine particulate matter and reflects cumulative health risk associated with all particulate substances in ambient air that fall into the particle size class of interest."[12]

Unlike in the ecological risk assessment for secondary NAAQS, EPA's risk assessment strategy as it is currently practiced for primary NAAQS is not responsive to cumulative risk factors such as other pollutants that co-occur with the specific CAPs under consideration. We are asking EPA to extend this approach and consider the additionality of impact on any health endpoint from other pollutants.

For example, ozone and $PM_{2.5}$ co-occur in ambient air and would be expected to have additive effects on specific health endpoints which they share (Fig 1).

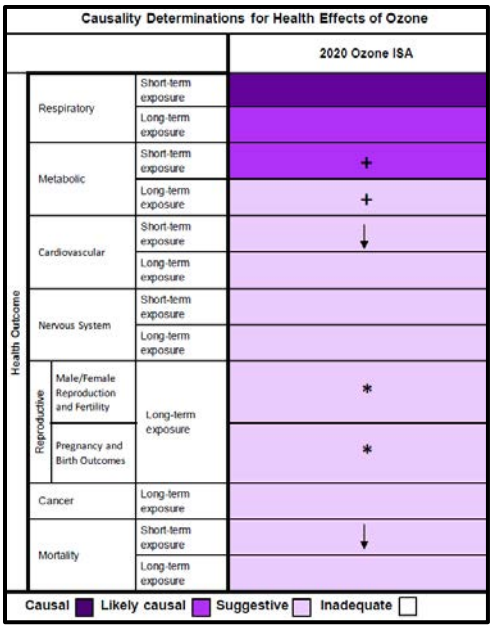

Table 2-1 ***Causal*** **and** ***likely to be causal*** **causality determinations for short- and long-term $PM_{2.5}$ exposure.**

Size Fraction	Health Effects Category	Exposure Duration	Causality Determination	Section
$PM_{2.5}$	Respiratory	Short-term	Likely to be causal	2.1.1.1.1
		Long-term	Likely to be causal	2.1.1.1.2
	Cardiovascular	Short-term	Causal	2.1.1.2.1
		Long-term	Causal	2.1.1.2.2
	Nervous system	Long-term	Likely to be causal	2.1.1.3.1
	Cancer	Long-term	Likely to be causal	2.1.1.4.1
	Mortality	Short-term	Causal	2.1.1.5.1
		Long-term	Causal	2.1.1.5.2

$PM_{2.5}$ = particulate matter with a nominal mean aerodynamic diameter less than or equal to 2.5 µm.

Figure 1 Causality determinations of specific health endpoints from exposures to ozone (left panel; data source: 2020 Ozone ISA) and $PM_{2.5}$ (right panel; data source: 2022 Supplement to the 2019 PM ISA). The exposure responses of these co-occurring CAPs need to be considered cumulatively in determining their NAAQS.

"A recent Canadian study…states that "Associations between Ox and mortality were consistently stronger in regions with elevated $PM_{2.5}$ transition metal/sulfur content and oxidative potential.""[13] As Dr. Frederick Lipfert, an independent consultant and a non-CASAC member responding to written questions from the 2020 ozone CASAC panel, pointed out, "Ozone never

[11] EPA's Guidelines for Cumulative Risk Assessment (May, 2023). Appendix A-6
[12] EPA's Guidelines for Cumulative Risk Assessment (May, 2023). Appendix A-6
[13] CASAC. (11/22/2022). Review of the EPA's ISA for Ozone; George A. Allen comment, pages 31-33

exists in isolation; co-pollutant effects must be considered with different exposure models" and in assessing its health risks. [14] This is also true for other CAPs.

Throughout various science assessments for NAAQS determinations, the Lung Association has raised objections to over-reliance on lab studies and dose-response chamber studies, in part because they examine the effects of a pure CAP which does not capture other members of its group that it represents (e.g. ozone for all photochemical oxidants, NO_2 for nitrogen oxides group, SO_2 for sulfur oxides mixture)[15] nor do they capture other unrelated pollutants (other CAPs) in ambient air whose health effects are well established.[16]

As a CASAC member, Ed Avol, clearly articulated in his assessment of EPA's draft policy assessment for the 2022 ozone NAAQS reconsideration: "A recurring shortfall of virtually all NAAQS reviews has been the lack of acceptance and strategy to address multi-pollutant co-exposures. Rarely do real-world ambient exposures occur one pollutant at a time. Based on both clinical and epidemiological research, other co-pollutants can serve to increase the impact or intensity of response. Acknowledgement of this more realistic exposure scenario would seem appropriate. In the regulatory context of reviewing individual criteria pollutants under the Clean Air Act, one approach to address multi-pollutant exposures might be to consider other contaminants as potential risk factors that could elevate or decrease exposure risk, much as SES, occupation, life stage, race, pre-existing disease, et cetera are considered in assorted reviews."[17]

In its consensus responses to charge questions on EPA's policy assessment in the recent $PM_{2.5}$ NAAQS reconsideration, this CASAC panel also recommended the consideration of cumulative risks of the mixture of pollutants in ambient air when reviewing NAAQS: "Consider the estimation of cumulative risk and impacts on health morbidity and mortality. There is increasing evidence that risk is cumulative and methods to estimate this risk are improving. In addition, the relationships between multiple exposures or co-pollutants, modifiers and outcomes (e.g., demographic, socioeconomic, built environment factors) should also be incorporated or acknowledged as sources of uncertainty."[18]

Cumulative assessment of health effects of pollutants that co-occur with a CAP would address the uncertainty from or confounding of these co-pollutants on the CAP exposure responses (to human health) as their impacts would be included in causality determinations instead of being controlled for or excluded. EPA's current health impacts assessment strategy in NAAQS policy "under-emphasizes the combined impact of various health findings by (1) under-valuing research findings from real-world multi-pollutant exposures, and (2) not considering the cumulative weight of additional susceptibility and vulnerability factors present in large segments of the population at large."[19] A comprehensive assessment that includes cumulative impacts of socioeconomic and sociodemographic factors, in addition to co-pollutants, would also more

[14] CASAC. (2/19/2020). Review of the EPA's Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards (External Review Draft); EPA-CASAC-20-003; page 101
[15] CASAC. (11/22/2022). Review of the EPA's ISA for Ozone; EPA-CASAC-23-001
[16] CASAC. (6/9/2023). Review of the EPA's Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2), EPA-CASAC-23-002
[17] CASAC. (6/9/2023). Review of the EPA's PA Draft Version 2 for Ozone NAAQS Reconsideration; page 60
[18] CASAC review of PM PA. (Nov 22, 2022), page 11.
[19] CASAC. (6/9/2023). Review of the EPA's PA Draft Ver2 for Ozone NAAQS Reconsideration; Ed Avol, page 60

clearly define the "adequate margin of safety to protect vulnerable populations" requirement of Clean Air Act in setting NAAQS.[20]

EPA should also consider cumulative health endpoints from CAP exposure, *i.e.* focus on "the combined strength of identified negative health outcomes across several organ system indices (respiratory, cardiovascular, neurologic, reproductive, metabolic)" instead of on "individual organ system uncertainties".[21]

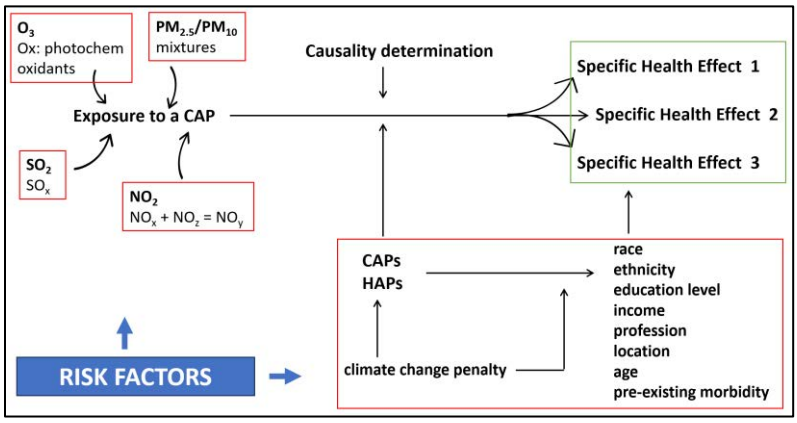

Figure 2 A directed acyclic graph showing multiple risk factors that influence causal determination of specific health endpoints from CAP exposures. The red blocks show risk factors that should be considered cumulatively and the green block shows health endpoints which also need to be assessed cumulatively in determining NAAQS.

A holistic cumulative approach that factors (Fig. 2) would truly reflect the impacts of the CAP rather than under-emphasize them as the current approach does.

CAP exposure responses are nuanced and complicated by more factors than are assessed by the simple 1-1 cause-effect approach that EPA currently uses. They warrant the use of cumulative impacts assessment in causality determinations, in health impact assessment, and in cumulative exposure risk assessment (*i.e.* "An analysis, characterization, and possible quantification of the combined risks to health and/or the environment from multiple agents and/or stressors"[22]) all of which underlie policy assessment which informs the level and form of the standard to be set.

CRA is both suitable and feasible in setting NAAQS since multiple factors compound the risk posed by the original CAP stressor on human health. EPA must therefore integrate CRA in its NAAQS review process and plan to use in its NAAQS determinations for CAPs.

[20] Clean Air Act. 42 U.S. Code § 7409, Section 109 - National primary and secondary ambient air quality standards
[21] CASAC. (6/9/2023). Review of the EPA's PA Draft Ver2 for Ozone NAAQS Reconsideration; Ed Avol, page 59
[22] EPA's Guidelines for Cumulative Risk Assessment (May, 2023). GLOSSARY OF KEY TERMS; page v