April 14, 2023

Comments to EPA on the Policy Assessment for the Reconsideration of the Ozone National Ambient Air Quality Standards, External Review Draft Version 2 (Draft PA)

Docket ID #: EPA-HQ-OAR-2018-0279

To protect public health from the impacts of ozone pollution, especially of people with lung disease and other at-risk populations, the American Lung Association has consistently called to revise the primary ozone NAAQS from the current 70 parts per billion (ppb) to a level that accurately reflects current science. The Lung Association offers the following comments on EPA's revised draft Policy Assessment in the reconsideration of the primary National Ambient Air Quality Standards (NAAQS) for Ozone.

Contents

I. EPA's preliminary conclusions on the primary ozone standard

On the CASAC charge question for review of the draft PA,[1] *"What are the Panel's views on the approach to considering the health effects evidence and the risk assessment to inform preliminary conclusions on the primary standard? To what extent is the evaluation of the available information, including the key considerations as well as associated limitations and uncertainties, technically sound and clearly communicated?"* we offer the following comment:

Science underlies causality determinations and risk assessments, which then inform policy. Limiting the scope of relevant scientific literature that is reviewed means that exposure risk assessment is constrained from limited data. This undermines the formulation of accurate and comprehensive policy in setting NAAQS to adequately protect public health.

In this second draft Policy Assessment (PA), EPA has again concluded that the current primary ozone NAAQS is adequate to protect human health with a margin of safety to protect vulnerable groups. This conclusion was informed by ignoring health effects evidence from population and epidemiological studies, by downgrading causality determinations, and by preferentially weighting controlled human exposure and chamber studies over other types of studies in both the Integrated Science Assessment (ISA) and the PA.

EPA did not consider all relevant studies in scientific literature in the ozone ISA. By applying the ill-defined criteria of its Population, Exposure, Comparison, Outcome, and Study Design (PECOS) tool arbitrarily and inconsistently, the agency limited its review of research to only

[1] EPA (Mar 1, 2023). Transmittal Memo - CASAC Review of the document titled Policy Assessment for the Reconsideration of the Ozone National Ambient Air Quality Standards, External Review Draft, Version 2

those studies that were conducted on geographic locations in the U.S. and Canada, while dismissing well-conducted and scientifically robust studies from the rest of the world.

EPA needs to reconsider the current framework of PECOS tool and its application in deciding the inclusion/exclusion of ISA-relevant studies. The National Academies (NAS) report on the Causality Framework raised concerns about the design and application of PECOS[2]: "Precise definition (such as provided by PECOS) of what evidence is considered relevant, and what aspects of studies are considered to enhance their quality, clarify the process and provide transparency" and "(s)uch definitions require review and revision by experts *(e.g., for ISAs by CASAC-EPA interaction)*… (e)xternal critical review and achieving consensus with reviewers enhances the robustness of the process, and the current ISA Preamble frameworks explicitly require such review. This is particularly critical for the definitions used (e.g., again the PECOS), for the application of quality criteria, and the synthesis of the evidence. The process requiring iterative CASAC and public review followed by EPA response and revision provides an important mechanism for providing transparency and garnering consensus in the NAAQS process, including in determining causal relationships."[3]

Additionally, this CASAC panel expressed "concerns about transparent and uniform application of eligibility criteria for study inclusion and about differential application of geographical location across health endpoints and exposure durations in determining study eligibility for consideration."[4] Also, as CASAC members pointed out, "it is unclear…why the PECOS criteria for 'study location' differs between the short-term and long-term assessments in the 2020 ISA." Further, "exclusion of well-designed and performed epidemiological research in non-North American populations limits the thoughtful application of scientific data that could be used to refine and improve understanding of primary and secondary health and material impacts."[5] Members of this CASAC panel pointed out that "(o)zone, unlike PM, is a pure chemical and its health effects should be the same throughout the world" and as such (dis)similarity of geographic locations or precursor emission sources should not be a factor in considering studies from across the world.

EPA's arbitrary and inconsistent application of the poorly designed PECOS tool, down-weighting of epidemiological studies, and disproportionate reliance on controlled human exposure studies resulted in the agency's inaccurate determinations of causality of health endpoints from short- and long-term ozone exposure, including:

1. Conclusions on cardiovascular effects

EPA downgraded causality determinations for cardiovascular effects and all-cause mortality effects from short-term ozone exposures from "likely causal" in the 2015 review to "suggestive of, but not sufficient to infer" based on controlled human exposure studies in the most recent ISA.[6] The agency's rationale for this change: "The number of controlled human exposure studies showing little evidence of ozone induced cardiovascular effects has grown substantially" and "the plausibility for a relationship between short-term ozone exposure to

[2] National Academies of Sciences, Engineering, and Medicine (Oct, 2022) Advancing the Framework for Assessing Causality of Health and Welfare Effects to Inform National Ambient Air Quality Standard Reviews. ISBN: 978-0-309-69011-9; Sponsor: EPA
[3] National Academies' Report on Causality Framework (Oct, 2022). page 88
[4] CASAC review of ozone ISA. (Nov 22, 2022), page 14 (5)
[5] CASAC review of ozone ISA. (Nov 22, 2022). pages 65 (A-36), 40 (A-11)
[6] EPA. (Apr, 2020). Integrated Science Assessment for Ozone and Related Photochemical Oxidants – Final Report. EPA/600/R-20/012; page 7, Table ES-1 Summary of causality determinations by exposure duration and health outcome.

cardiovascular health effects is weaker than it was in the previous review, leading to the revised causality determination."[7]

Controlled human exposure studies are experiments conducted with pure ozone for a short duration on a small number of study subjects who are healthy young adults, while epidemiologic studies involve large cohorts that include vulnerable and sensitive groups. Epidemiologic studies also more accurately capture exposures to ambient ozone, and other photochemical oxidants that it is an indicator of for the setting of NAAQS. Because controlled human exposure studies do not represent the population at large and do not represent the photochemical soup in the ambient air that people are exposed to, they underestimate health effects (including cardiovascular and respiratory effects) from ambient ozone exposures. EPA's reliance on controlled human exposure findings to the exclusion of epidemiologic data, and extrapolating those findings to all demographics in reaching policy conclusions, is flawed.

EPA further rejects the existence of "consistent or generally consistent evidence for a limited number of O_3-induced cardiovascular endpoints in animal toxicological studies and cardiovascular mortality in epidemiologic studies".[8] However, there are several epidemiologic studies, which under the application of the current PECOS criteria would be excluded from consideration, that provide strong evidence of association of ozone exposure with cardiovascular health. One such study was just published by a group of Chinese and American researchers on Chinese population cohorts (6.5 million hospital admissions) that shows linkage between ozone pollution and hospital admissions for cardiovascular events.[9] Another article in the same issue of the journal by European scientists offers insight into the mechanisms of the biological effects of ozone on cardiovascular mortality and cardiovascular morbidities, including hypertension, coronary ischemia, and impairment of autonomic control.[10]

2. Conclusions on respiratory effects

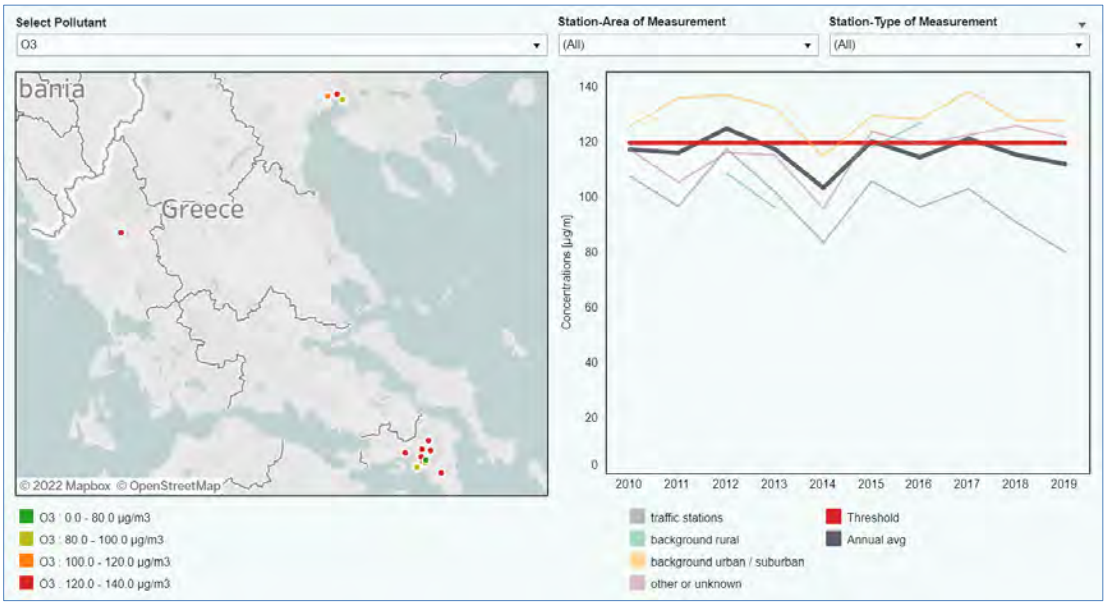
EPA concluded that there are no symptomatic respiratory effects in vulnerable and sensitive groups from short-term O_3 exposure below the current standard based on controlled human exposure studies, citing "findings from controlled human exposure studies of healthy subjects at the benchmark 60 ppb [parts per billion] concentration which showed statistically significant decrements in lung function but not respiratory symptoms, including one study which showed a statistically significant increase in a biomarker of airway inflammatory response relative to filtered air exposures."

Brown *et al*. (2008)[11] showed that a 60 ppb exposure of healthy subjects causes a highly statistically significant decrease in mean FEV(1) responses.[12] EPA's own researchers, Kim *et al*. (2011), found that "exposure of healthy young adults to 0.06 ppm ozone for 6.6 hours causes a significant decrement of FEV1 and an increase in neutrophilic inflammation in the airways."[13] This significant decrease in lung function and increased airway inflammation among

[7] EPA. (Mar, 2023). Policy Assessment for the Reconsideration of the Ozone National Ambient Air Quality Standards - External Review Draft Version 2, EPA-452/P-23-002; page 118
[8] EPA. (Mar, 2023). Policy Assessment Draft Version 2, EPA-452/P-23-002; page 125
[9] Jiang, Y., *et al*. (Mar 10, 2023). Ozone pollution and hospital admissions for cardiovascular events. *European Heart Journal*, ehad091
[10] Münzel, T., Hahad, O., & Daiber, A. (Mar 10, 2023). The emergence of the air pollutant ozone as a significant cardiovascular killer? *European Heart Journal*, ehad046.
[11] Brown, J. S., Bateson, T. F., & McDonnell, W. F. (2008). Effects of exposure to 0.06 ppm ozone on FEV1 in humans: a secondary analysis of existing data. *Environmental health perspectives*, *116*(8), 1023–1026.
[12] Spirometry: Procedure, "Normal" Values, and Test Results. Forced expiratory volume (FEV1) is the amount of air a person can force from the lungs in one second. It is measured during a pulmonary function test (also called spirometry test) and used in the diagnosis of COPD.
[13] Kim, C. S., *et al*. (2011). Lung Function and Inflammatory Responses in Healthy Young Adults Exposed to 0.06 ppm Ozone for 6.6 Hours. *American Journal of Respiratory and Critical Care Medicine, 183*(9).

healthy subjects could translate to much more severe respiratory illnesses with symptoms among at-risk populations such as children, elderly people, and people with existing pulmonary issues (e.g. asthma), Since direct dose-response/exposure measurements of sensitive groups are not obtainable, EPA must consider this rationale as biologically probable and plausible in inferring causality of respiratory effects[14] at 60 ppb exposure.

Among the studies that would be ineligible for consideration under the PECOS framework is a recent panel study (Respiratory Effects of Ozone Exposure in children; RESPOZE) in two Greek cities with ambient ozone concentrations higher than the EU standard of 49.1 ppb (see graphic below).[15] Using fixed site measurements and modeling calibrated for personal exposures, the researchers evaluated the respiratory health effects of long-term ozone exposure in 10-11-year old schoolchildren. The study showed that a 5 ppb increase in ambient ozone is associated with reduced lung volumes (FVC and FEV1) and decreases in lung growth over the study period.



[16]

Another (PECOS-ineligible) recent study from China[17] analyzed the impacts of low level O_3 exposure on asthma-related hospitalizations in a cohort of 3,475 children. Using air pollution and meteorological data, they employed a case-crossover design and conditional logistic regression analyses to evaluate the association between asthma attacks and outdoor air pollution with lag structures in both single and multi-pollutant models. They estimated the impacts of ozone exposure on an asthma attack at three maximum daily 8-hour sliding average ozone concentrations of ≥50 ppb, 40-50 ppb, and <40 ppb. The study showed that ozone concentration above 40 ppb contributed to an increased risk of acute asthma attacks on each day of lag, in both single- and multi-pollutant models.

[14] "An inference of causality is strengthened by results from experimental studies or other sources demonstrating biologically plausible mechanisms. A proposed mechanism, which is based on experimental evidence and which links exposure to an agent to a given effect, is an important source of support for causality." Integrated Science Assessment for Oxides of Nitrogen – Health Criteria

[15] Dimakopoulou, K., *et al*. (2020). Long-term exposure to ozone and children's respiratory health: Results from the RESPOZE study. *Environmental research*, *182*, 109002

[16] https://www.eea.europa.eu/themes/air/country-fact-sheets/2021-country-fact-sheets/greece

[17] Huang, W., Wu, J., & Lin, X. (2022). Ozone Exposure and Asthma Attack in Children. *Frontiers in pediatrics*, *10*, 830897

In summary, evidence from multiple peer-reviewed international studies including epidemiologic and population studies since 2015 implicate ozone exposure as a causal agent in cardiovascular and respiratory morbidities and related mortality. These data strongly support revising the current 70 ppb ozone NAAQS set in 2015 to lower than 60 ppb to protect public health with an adequate margin of safety.

3. Down-weighting epidemiologic studies instead of considering them in the context of cumulative impacts from multiple pollutants

Epidemiologic studies, especially those that use single pollutant exposure models for ozone impacts analyses, will always have some degree of uncertainty caused by confounding multiple pollutants present in the ambient air alongside which ozone exists. It is precisely in cases such as these that EPA needs to err on the side of protecting health. The Clean Air Act requires EPA to include an adequate "margin of safety" in setting the NAAQS, which the Agency interprets thus: "(t)he requirement that primary standards provide an adequate margin of safety was intended to address uncertainties associated with inconclusive scientific and technical information available at the time of standard setting."[18] The precautionary principle demands that EPA set the ozone NAAQS at a level that accounts for health effects on vulnerable groups from cumulative exposure to multiple pollutants.[19]

Ozone occurs in a mixture of air pollutants which are all hazardous to human health, either directly or indirectly. Some of these co-pollutants are highly correlated and associated with each other and could also have additive effects on health. Qualitative and quantitative analyses of the morbidity/mortality burden attributable to specific pollutants using a single pollutant exposure model would therefore always have some degree of uncertainty due to confounding co-pollutants, as epidemiological studies over the past two decades have shown. If several pollutants are highly correlated with each other, and if each one has an effect on morbidity or mortality, then the statistical association of each individual pollutant with morbidity or mortality would also reflect the effects of other pollutants in the group.

Instead of identifying attribution of specific health effects to individual pollutants from a multipollutant mixture, EPA should consider the cumulative impacts of the entire pollutant mixture in determining the ozone NAAQS. In an article in *Pace Environmental Law Review*, Prof. Deborah Behles observed more than a decade ago that "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."[20]

"EPA should evaluate and consider cumulative health impacts when it reviews and revises ozone NAAQS 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."[21]

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[18] EPA. (Apr, 2020). Integrated Science Assessment for Ozone and Related Photochemical Oxidants – Final Report. EPA/600/R-20/012

[19] European Parliament (Sep 12, 2015). Think Tank: The precautionary principle: Definitions, applications and governance - In-Depth Analysis

[20] 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*.

[21] Behles, D. N. (2010). *28 Pace Envtl. L. Rev. 200*.

EPA's own 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".[22] This study also finds that because the two grants of authority from the Clean Air Act in setting NAAQS, i.e. "requisite to protect the public health" while "allowing an adequate margin of safety" are distinguishable, the courts upheld "EPA's interpretation of its authority to consider any information or analyses the Agency reasonably determines is necessary to decide the level at which standards are protective of the public health."[23]

Consideration of cumulative impacts is also among the recommendations of one of the CASAC members who noted that in the PA, EPA "under-emphasizes the impacts of ozone on human health" by not considering cumulative impacts. In this context, the member makes two important points:

i. "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 *(socioeconomic status)*, occupation, life stage, race, pre-existing disease, et cetera are considered in assorted reviews."
ii. "Focusing on individual organ system uncertainties more than on the combined strength of identified negative health outcomes across several organ system indices (respiratory, cardiovascular, neurologic, reproductive, metabolic)" underemphasizes the total health effects of ozone exposure. "The presented data collectively lays a foundation for the Administrator to consider a more restrictive standard at or below 60 ppb for eight hours"[24]

Therefore, we ask EPA to consider cumulative impacts of copollutants in revising the level of ozone NAAQS to a range of 60 – 55 ppb, as advised by the overwhelming majority of CASAC.[25]

II. Requirement and need for potential alternative standards

In concluding that the current primary ozone NAAQS is sufficient to protect human health with an adequate margin of safety to protect vulnerable subpopulations, EPA avoided having to provide the Administrator with potential alternative standards and comprehensive data required for his deliberations.

The ozone panels of CASACs from several previous ozone NAAQS reviews consistently advised EPA to revise the primary standard to a range down to 60 ppb.

The 2006 "CASAC unanimously recommends that the current primary ozone NAAQS be

[22] Alves, S., Tilghman, J., Rosenbaum, A., & Payne-Sturges, D. C. (2012). U.S. EPA authority to use cumulative risk assessments in environmental decision-making. *International journal of environmental research and public health*, *9*(6), 1997–2019.
[23] Alves *et al*. (2012). U.S. EPA authority to use cumulative risk assessments in environmental decision-making.
[24] Clean Air Scientific Advisory Committee (CASAC). (Mar 27, 2023). Preliminary Draft Comments from Members of CASAC Ozone Panel on EPA's Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2); pages 7-8
[25] Alves *et al*. U.S. EPA authority to use cumulative risk assessments in environmental decision-making.

revised and that the level that should be considered for the revised standard be from 0.060 to 0.070 ppm, with a range of concentration-based forms from the third- to the fifth highest daily maximum 8-hr average concentration. While data exist that adverse health effects may occur at levels lower than 0.060 ppm, these data are less certain and achievable gains in protecting human health can be accomplished through lowering the ozone NAAQS to a level between 0.060 and 0.070 ppm."[26]

The 2011 CASAC: "(W)e reaffirm that the evidence from controlled human and epidemiological studies strongly supports the selection of a new primary ozone standard within the 60 – 70 ppb range for an 8-hour averaging time."[27]

The 2015 "CASAC deliberated at length regarding advice on other levels that might be considered to be protective of public health with an adequate margin of safety. For example, the recommended lower bound of 60 ppb would certainly offer more public health protection than levels of 70 ppb or 65 ppb and would provide an adequate margin of safety. Thus, our policy advice is to set the level of the standard lower than 70 ppb within a range down to 60 ppb, taking into account your judgment regarding the desired margin of safety to protect public health, and taking into account that lower levels will provide incrementally greater margins of safety."[28]

Over the past decade and a half since, the science warranting a more protective standard has only become stronger with overwhelming collective evidence from both controlled human exposure experiments and epidemiologic studies which shows that there is no threshold exposure level at which there is no adverse health effect. The current CASAC panel accordingly advised EPA in a near-unanimous (17-1) recommendation that the primary ozone standard be set within the range of 60-55 ppb to adequately protect public health with an adequate margin of safety to protect sensitive and at-risk subpopulations.[29] We very strongly support this recommendation and urge EPA to provide the Administrator with this range of concentrations for his deliberations in setting the ozone NAAQS.

III. EPA's document presentation for public input

We submitted the following comment to the earlier version of the draft PA in June, 2022 and are obliged to reiterate it here since it was not addressed by the EPA in the current draft PA: "To enable meaningful public comment, especially given the tight deadlines to review the 1,000+ pages of the PA, EPA should improve the presentation and organization of the document… In all its documents, EPA should internally hyperlink sections, figures, and tables to make them clickable." [30] We observed again in our comment submitted on March 22, 2023 the need for a table of contents in voluminous public documents.[31] We are pleased to note that members of the current CASAC panel have also made similar recommendations[32] stressing the need for a

[26] CASAC. (2006). Peer Review of the Agency's 2nd Draft Ozone Staff Paper. EPA-CASAC-07-001; page 5
[27] Letter from Dr. Jonathan M. Samet, Chair, Clean Air Scientific Advisory Committee, to Lisa P. Jackson, Administrator, U.S. Environmental Protection Agency, March 30, 2011
[28] CASAC. (2014). Review of the EPA's Second Draft Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards, EPA-CASAC-14-004; pages 2-3
[29] CASAC (2023). Ozone Review Panel Public Meeting March 29 – 30;
Day 1: https://www.youtube.com/live/kHDedV0ELnw?feature=share,
Day 2: https://www.youtube.com/live/kHDedV0ELnw?feature=share
[30] ALA comment (Jun, 2022). EPA's Policy Assessment for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review), Docket: EPA-HQ-OAR-2018-0279-0600; Tracking #: l3u-nhnl-kl55
[31] CASAC (2023). Ozone Review Panel Public Meeting March 29; Presentation by Registered Public Speaker - Oral Statement from Shyamala Rajan, American Lung Association
[32] Clean Air Scientific Advisory Committee (CASAC). (Mar 27, 2023). Preliminary Draft Comments on PA (External

table of contents with page numbers, internal bookmarks, a list of tables, and a list of figures in the lengthy PA.

"EPA should also make in-text citations/footnotes and the URLs in the references clickable. These structure and formatting changes would improve stakeholders' ability to review and respond to the document."[33]

We expect the above cited elements to be standard features in any document that EPA publishes on any issue. Anything less from an agency whose job it is to protect public health is ill-serving the public if the public cannot easily engage in the regulatory processes.

IV. Prompt conclusion of this reconsideration process

EPA anticipates that this ozone NAAQS reconsideration process cannot be completed any more expeditiously than the end of 2024 based on "the time that was necessary for the CASAC to complete its science review, the time that EPA needed to update the draft PA" and steps to follow. In this reconsideration, the EPA did not prepare a new ISA and CASAC deliberations on the science concluded last year. Following CASAC's final review of the draft policy assessment at the end of May 2023, EPA has three remaining steps - developing a final PA, guided by CASAC advice and public comments, then proposing and later finalizing its decision after considering public comment. There is absolutely no justification for extending these last steps for nearly two years. Delaying the final decision until the end of 2024 will adversely affect public health not only in this review but into the long future as it will delay future NAAQS reviews on the 5-year cycle.

We therefore ask EPA to conclude this reconsideration process no later than April 2024.

V. Conclusion

The American Lung Association works on behalf of everyone's lung health, but particularly serves populations with lung diseases such as lung cancer, asthma, and COPD. We also place a heavy emphasis on the lung health of children and of seniors, because people under 18 and over 65 are at greater risk of harm to the lungs from a variety of sources. These sub-populations and those with existing morbidities, groups of lower socioeconomic status, people of color are all at greater risk of health harm from ozone pollution exposure.

The Clean Air Act directs EPA to ensure that these populations are protected from ozone pollution. EPA's heavy reliance on controlled human exposure studies in the draft Policy Assessment falls far short of this requirement, as does its effort to discount existing epidemiological evidence on cardiovascular and respiratory impacts and its failure to consider the impacts of cumulative exposure from ozone as part of a mix of air pollutants.

We urge you to follow the science and the law, and the advice of the CASAC, in recommending that the Administrator set the level of primary ozone NAAQS in the range of 60-55 ppb to adequately protect public health with a margin of safety for at-risk groups.

Review Draft Version 2); CASAC Ozone Review Panel Public Meeting March 29: https://www.youtube.com/live/kHDedV0ELnw?feature=share

[33] ALA comment (Jun, 2022). EPA's Policy Assessment for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review), Docket: EPA-HQ-OAR-2018-0279-0600; Tracking #: l3u-nhnl-kl55