DATE

EPA-CASAC-23-XXX

The Honorable Michael S. Regan
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Subject: CASAC Review of the EPA's *Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2)*

Dear Administrator Regan:

The 2022 Clean Air Scientific Advisory Committee (CASAC) Ozone Review Panel, hereafter referred to as the Panel, met on March 2, 2023, March 29-30, 2023, and May 23-24, 2023, to peer review the EPA's *Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2)*, hereafter referred to as the PA. The Chartered CASAC approved the Panel's report on <<Insert date of approval>>. The CASAC's consensus responses to the charge questions and the individual review comments from the Panel are enclosed.

The PA clearly presents background and historical information, which provides useful context for the reconsideration. It would be helpful to provide additional detail on how the CASAC's comments on the 2020 Ozone Integrated Science Assessment (ISA) factored into the PA, particularly the health effects chapters. The CASAC notes that in the past several National Ambient Air Quality Standards (NAAQS) reviews, Risk and Exposure Assessments (REAs) have been incorporated into the PAs as appendices, rather than developed as standalone documents. For future NAAQS reviews, the CASAC recommends that REAs be developed as separate standalone documents and should be reviewed by the CASAC prior to the development of PAs.

The PA provides a clear presentation of information on air quality. It should clearly state if methane is included in the volatile organic compound emissions discussed in the PA. Although the PA includes a presentation of U.S. Background (USB), the CASAC did not find a clear discussion of how USB is relevant for decisions in setting the NAAQS and found the discussion of the legislative requirements on the role of background to be inadequate. The CASAC recommends that the EPA clearly state how USB can and cannot be considered in setting the NAAQS.

The CASAC finds that the PA summarizes a wide breadth of information and clearly communicates the EPA's conclusions regarding the current primary standard for ozone. A large amount of data was collected and analyzed for the ISA, however, the CASAC believes this wealth of information was not fully utilized in the PA. All CASAC members,* except for one, are concerned that the approach taken in the PA may substantially underestimate public health risk. The presented rationale for relying on the controlled human exposure (CHE) data is strong, but the exclusion of consideration of the epidemiological data is concerning. Since the NAAQS primary standard is for ozone and other photochemical oxidants, this merits inclusion of epidemiological studies that are not restricted to ozone exposure alone. There is no scientific evidence that CHEs, as an independent line of evidence, are inherently more informative than epidemiological data, yet the PA prioritizes their value in informing the adequacy of the public health protection afforded by the ozone standard. The CASAC recommends a rebalancing of the presentation regarding CHE studies and epidemiological studies to address the inherent limitations in CHEs in determining a lower bound for the level of the standard as well as to incorporate the information available from the epidemiological studies. Regarding at-risk populations, extrapolating CHE studies with adult participants to apply to children requires a strong justification and more thorough explanation. The absence of children from the reviewed CHE studies (and in the literature) is an appreciable data limitation and therefore, cannot be used in risk estimation directly. The PA states that outdoor workers are omitted due to appreciable data limitations and the CASAC finds this explanation to be insufficient. Ignoring this at-risk group may result in an underestimate of the adverse impact to the public.

The CASAC agrees that retaining ozone as the indicator is appropriate, and that there is inadequate evidence to support changes in the averaging time or form of the standard. However, it is suggested that future reviews examine the impacts of alternate forms and averaging times in conjunction with the level.

All of the CASAC members,* except for one, conclude that the scientific evidence indicates that the level of the current primary standard is not sufficiently protective of public health. CHE studies demonstrate adverse effects in healthy adults at or below the current standard of 70 ppb. The 6.6-hour CHE studies with exercise show airway inflammation, decrements in lung function, and increased symptoms at 70 ppb. Hernandez et al. (2021) observed airway effects at 70 ppb without exercise, and Kim et al. (2011) demonstrated airway effects at 60 ppb with exercise. All of these studies were performed in healthy adults and there are no 6- to 7-hour CHE studies which evaluated children or people with asthma, where adverse effects would be expected to be greater. Panel studies such as Korrick et al. (1998) indicate that people with asthma or wheeze may experience greater adverse effects from exposure to ambient ozone than healthy people. The epidemiological studies provide convincing evidence of increases in childhood emergency department visits and hospital admissions for asthma in association with ozone exposures well below the current standard. For example, Strickland et al. (2010)

* This also includes all of the CASAC Ozone Panel members, except for the one CASAC member.

showed increases in asthma ED visits associated with ozone exposure concentrations between 45 and 65 ppb.

All of the CASAC members,* except one, recommend a level in the range of 55 to 60 ppb to be protective of public health. This scientific judgement is based on consideration of all of the scientific evidence, including CHE studies, epidemiological studies, and animal studies, and considering the need to protect children, people with asthma, outdoor workers, and other at-risk populations. The CASAC acknowledges that the choice of a level within the scientifically recommended range is a policy judgment and that the lower end of the range would offer more of a margin of safety and the upper end of the range would provide less of a margin of safety.

One CASAC member, however, concurs with the EPA that the available evidence and exposure/risk information do not call into question the adequacy of protection provided by the existing standard and that it should be retained without revision. At a standard of 70 ppb, the REA estimates that more than 99% of children with asthma are protected from a single exposure at/above 70 ppb and more than 95% of children with asthma are protected from experiencing multiple exposures at/above 60 ppb. This member believes that, under the assumptions made in the PA, the current standard will provide adequate protection at concentrations well below the level of the standard. A REA using concentration-response functions from epidemiological studies was not conducted and therefore, the PA is limited in its ability to use epidemiological studies to provide insights regarding health outcomes that might be expected under air quality conditions that meet the current and alternative standards.

The CASAC unanimously recommends that future ozone REAs and PAs include consideration of health effects evidence from epidemiological and panel studies, and that the Population, Exposure, Comparison, Outcome, and Study Design (PECOS) study selection criteria in ISAs be broadened to include studies conducted outside of the U.S. and North America.

The PA provides detailed analyses of various welfare effects and the rationales for determining their levels of causality. These in turn are used to evaluate the efficacy of these measures for determining OZONE exposures that would provide the requisite protection of the public welfare. The CASAC finds that the PA provides excellent reviews of the degrees of causality for vegetation, ecosystems, and plant-insect interaction responses to ozone, but that the discussion of its influences on climate could be clarified and strengthened.

In the PA, the EPA concludes that the scientific evidence and quantitative air quality and exposure analyses support retention of the current standard, without revision. All of the CASAC members,* except for one, do not concur and find that the PA does not provide appropriate and sufficient rationale to support this conclusion with respect to the current secondary standard. Specifically, they find that the current secondary standard does not provide sufficient protection against the public welfare effects of ozone and other photochemical oxidants. Although the current standard is expected to result in lower severity and incidence of visible foliar injury, it does not provide sufficient protection against reduced growth effects in sensitive tree species and ecosystems, annual plants, and in crops of major importance to U.S. food security. The PA states that the current secondary standard is equivalent to a W126 index of

17 ppm-hrs, a level at which the median response of the combined studies results in a relative biomass loss (RBL) of less than 6%. However, the nonlinearity of the exposure-response relationship calls into question the use of the median value for this purpose. Additionally, the 3-year averaging time is based on analysis of RBL and does not include relative yield loss (RYL) of annual plants, including agricultural crops.

At a W126 index value of 17 ppm-hrs, the most recent data (Lee et al., 2022) show that nearly half (i.e., seven) of the 16 tree species for which exposure-response functions exist (species with a broad range throughout the U.S. and assumed to represent the range of ozone sensitivity for species without exposure-response functions) experience a RBL ranging from 9-29%, an effect that is compounded over time in long-lived species, such as trees. For annual crops, a W126 index value of 17 ppm-hrs results in RYL ranging from 6-12% for five of 10 crop species. Among these are three of the most important U.S. crops in terms of cash crop receipts (i.e., cotton, soybean, winter wheat). Because nearly half of species would be significantly affected at a W126 index value of 17 ppm-hrs, and because impacts on many other species remain unknown, these CASAC members do not find this level to be protective.

Based on the scientific evidence, all of the CASAC members,[*] except one, recommend a W126 index value of 7 - 9 ppm-hrs as the target level of protection, to protect against reduced growth in sensitive tree species and annual crops. Additionally, this would control for the effects of peak concentrations on plant growth. At this level of protection, RBL and RYL are ≤5% for the majority (>69%) of species. At 9 ppm-hrs, 69% of tree species and 100% of annual crop species with exposure-response relationships experience ≤5% RBL and RYL, respectively. At 7 and 8 ppm-hrs, >75% of tree species and 100% of annual crop species experience ≤5% RBL and RYL, respectively. This recommendation is comparable to an earlier 2014 CASAC recommendation "that the level associated with this form be within the range of 7 - 15 ppm-hrs to protect against current and anticipated welfare effects of ozone." This recommendation is also comparable to recommendations by the National Park Service (NPS) to use a lower benchmark value similar to that used by NPS, which describes 7 ppm-hrs to 13 ppm-hrs as "moderate conditions" for vegetation health. Finally, the recommendation is also consistent with the Lee et al. (2022) study that illustrates a maximum of 9.2 ppm-hrs to protect sensitive species at a 5% RBL level.

For the averaging time of the secondary standard, all of the CASAC members,[*] except one, suggest that the W126 be accumulated over a rolling 92-day window, and that the highest value be considered. With regards to the form, these CASAC members recommend a single year highest cumulative W126 index value not to be exceeded more than 2 years out of any 5-year interval. This accounts for interannual variability yet ensures that the target W126 index value is met in more years than not.

One CASAC member, however, concurs with the EPA that the body of evidence, and the quantitative air quality and exposure analyses presented in the PA do not call into question the adequacy of the protection provided by the current secondary standard and that it should be retained without revision. This member concurs with the EPA that the evidence provides support for use of a multiyear average in assessing the level of protection provided by the current standard from cumulative seasonal exposures related to RBLs of concern. The PA shows that the seasonal W126 index values (3-year average) are at or below 17 ppm-hrs when the current standard is met at all 877 monitoring locations that were examined. This member believes that the form and averaging time of the standard are not required to match those of the exposure metrics, as long as the standard, in all its elements, provides requisite protection against effects characterized for exposures of concern. Therefore, this member agrees with the EPA that the current 8-hour ozone standard can be used as a surrogate for the W126 exposure metric. In addition, this member believes that any recommendation for an alternative secondary standard should be evaluated in the proper context of the standard to determine the adequacy of the alternative standard.

For climate impacts of ozone, the CASAC finds that there is strong evidence that anthropogenic climate change is occurring, that elevated concentrations of ozone are important for global climate, and that emissions from the U.S. are contributing to that warming. However, the CASAC agrees with the EPA that it is not straightforward to relate concentrations of ozone at ground level with climate changes from ozone, and as such, the CASAC agrees that the basis is insufficient to support a secondary standard for ozone based on impacts on climate.

The CASAC also has recommendations on future research needs for both the primary and secondary standards, which are detailed in the consensus responses.

In summary, the CASAC appreciates the thorough review presented in the PA. However, all of the CASAC members,[*] except one, do not agree with the EPA's conclusions about the protectiveness of the primary and secondary standards because they do not agree with and have concerns with several pivotal decisions and assumptions in the analyses that the conclusions are based upon. New literature that is not included in the PA further questions some key assumptions presented in the PA. Regarding the primary standard, these CASAC members are concerned about the overreliance on CHE studies, limitations of using CHE studies to determine a lower bound for the level of the standard, limitations of CHE studies to extrapolate to at-risk populations (e.g., children, outdoor workers, people with asthma), exclusion of epidemiological studies, and recent CHE evidence demonstrating adverse effects at levels below the current standard in health young adults with exercise, and adverse effects at the level of the current standard in healthy young adults at rest. Regarding the secondary standard, these CASAC members do not agree with the use of median RBL values to determine the protectiveness of the current standard and find that recent scientific evidence indicates that the current secondary standard provides insufficient protection against reduced growth effects on sensitive tree species, ecosystems, annual plants, and crops of major importance to U.S. food security. Although the PA's use of the median value is based on CASAC advice in previous NAAQS reviews, the CASAC, after reviewing the analyses in the PA, along with newer and more robust literature on the effects of ozone on RBL, finds that the use of the median value is not supported. In conclusion, all of the CASAC members,[*] except one, conclude that the scientific evidence unequivocally demonstrates that the current primary and secondary standards are not protective of public health and public welfare, and that the scientific evidence supports their recommendations of alternative primary and secondary standards mentioned above and detailed in the consensus responses.

The CASAC wishes to acknowledge the value of its deliberative process, and expresses its appreciation for the opportunity to convene in person once again. The CASAC finds that in-person meetings lead to a more productive and effective dialogue than is possible when meetings are exclusively virtual. The deliberative process and multi-day in-person meeting format allows for development of a deeper and more refined collective understanding of the key scientific issues. Reiterating advice from the 2022 CASAC review of the Particulate Matter ISA Supplement, the CASAC commends the EPA for returning to its long-standing practice of constituting an ad hoc panel of experts to complement the expertise of the Chartered CASAC. The CASAC recommends that the practice of convening a panel of additional experts continue for all future NAAQS reviews because the give-and-take deliberation and participation of multiple scientific experts, including multiple experts from all key disciplines needed to conduct a high-quality scientific review, is fundamental to the Chartered CASAC's ability to provide the highest quality scientific advice. With a fully constituted ad hoc panel of experts, the CASAC has a broad depth and breadth of perspectives that enables it to fulfill its mandate to provide advice and recommendations to the EPA.

The CASAC appreciates the opportunity to provide advice on the PA and looks forward to the agency's response.

Sincerely,

Dr. Elizabeth A. (Lianne) Sheppard, Chair
Clean Air Scientific Advisory Committee

Enclosures

NOTICE

U.S. Environmental Protection Agency
Clean Air Scientific Advisory Committee

CHAIR

Dr. Elizabeth A. (Lianne) Sheppard, Rohm and Haas Professor in Public Health Sciences, Department of Environmental & Occupational Health Sciences and Department of Biostatistics, Hans Rosling Center for Population Health, University of Washington, Seattle, WA

MEMBERS

Dr. Michelle Bell, Mary E. Pinchot Professor of Environmental Health, Yale University School of the Environment, New Haven, CT

Dr. James Boylan, Assistant Branch Chief, Air Protection Branch, Environmental Protection Division, Georgia Department of Natural Resources, Atlanta, GA

Dr. Judith C. Chow, Nazir and Mary Ansari Chair in Entrepreneurialism and Science and Research Professor, Division of Atmospheric Sciences, Desert Research Institute, Reno, NV

Dr. Mark W. Frampton, Professor Emeritus of Medicine, Pulmonary and Critical Care, University of Rochester Medical Center, Rochester, NY

Dr. Christina H. Fuller, Associate Professor, School of Environmental, Civil, Agricultural and Mechanical (ECAM) Engineering, University of Georgia College of Engineering, Athens, GA

Dr. Alexandra Ponette-González, Associate Professor, Department of City & Metropolitan Planning, University of Utah, Salt Lake City, UT

SCIENCE ADVISORY BOARD STAFF

Mr. Aaron Yeow, Designated Federal Officer, U.S. Environmental Protection Agency, Science Advisory Board Staff Office, Washington, DC

U.S. Environmental Protection Agency
Clean Air Scientific Advisory Committee
Ozone Review Panel (2022)

CHAIR

Dr. Elizabeth A. (Lianne) Sheppard, Rohm and Haas Professor in Public Health Sciences and Professor, Department of Environmental & Occupational Health Sciences and Department of Biostatistics, Hans Rosling Center for Population Health, University of Washington, Seattle, WA

CASAC MEMBERS

Dr. Michelle Bell, Mary E. Pinchot Professor of Environmental Health, Yale University School of the Environment, New Haven, CT

Dr. James Boylan, Assistant Branch Chief, Air Protection Branch, Environmental Protection Division, Georgia Department of Natural Resources, Atlanta, GA

Dr. Judith C. Chow, Nazir and Mary Ansari Chair in Entrepreneurialism and Science and Research Professor, Division of Atmospheric Sciences, Desert Research Institute, Reno, NV

Dr. Mark W. Frampton, Professor Emeritus of Medicine, Pulmonary and Critical Care, University of Rochester Medical Center, Rochester, NY

Dr. Christina H. Fuller, Associate Professor, School of Environmental, Civil, Agricultural and Mechanical (ECAM) Engineering, University of Georgia College of Engineering, Athens, GA

Dr. Alexandra Ponette-González, Associate Professor, Department of City & Metropolitan Planning, University of Utah, Salt Lake City, UT

CONSULTANTS

Mr. George A. Allen, Chief Scientist, Northeast States for Coordinated Air Use Management (NESCAUM), Boston, MA

Mr. Ed Avol, Professor, Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA

Dr. Terry Gordon, Professor, Department of Medicine, Division of Environmental Medicine, New York University School of Medicine, New York, NY

Dr. Catherine J. Karr, Professor, Department of Pediatrics and Department of Environmental & Occupational Health Sciences, University of Washington, Seattle, WA

Dr. Michael T. Kleinman, Professor, Department of Medicine, Division of Occupational and Environmental Medicine, University of California, Irvine, Irvine, CA

Dr. Danica Lombardozzi, Climate and Global Dynamics Laboratory, National Center for Atmospheric Research, Boulder, CO

Dr. Howard Neufeld, Professor, Department of Biology, Appalachian State University, Boone, NC

Dr. Jennifer Peel, Professor and Section Head of Epidemiology, Department of Environmental and Radiological Health Sciences, Colorado State University, Fort Collins, CO

Dr. Richard Peltier, Associate Professor, Environmental Health Sciences, School of Public Health and Health Sciences, University of Massachusetts Amherst, Amherst, MA

Dr. Jeremy Sarnat, Associate Professor of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA

Dr. Jason West, Professor, Department of Environmental Sciences & Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC

SCIENCE ADVISORY BOARD STAFF

Mr. Aaron Yeow, Designated Federal Officer, U.S. Environmental Protection Agency, Science Advisory Board Staff Office, Washington, DC

Consensus Responses to Discussion Points on the EPA's *Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2)*

Chapter 1 – Introduction

1. To what extent does the Panel find that the information in Chapter 1 is clearly presented and provides useful context for this reconsideration?

The information in Chapter 1 is clearly presented and provides useful content for this reconsideration. The information on the history of the ozone National Ambient Air Quality Standards (NAAQS) reviews was well done and especially useful. The Clean Air Act sections that govern NAAQS revisions and subsequent court decisions that refine the requirements of a NAAQS review are clearly described and referenced.

Section 1.5 notes the EPA's provisional assessment memos from 2020 and 2022 as the basis for not reopening the 2020 air quality criteria review (i.e., the Integrated Science Assessment), and briefly describes the fall 2022 discussion of the 2020 Integrated Science Assessment (ISA) by the Clean Air Scientific Advisory Committee (CASAC). Although that discussion did not result in a CASAC recommendation that the 2020 ISA be reopened or revised, the CASAC did express concerns regarding some aspects of the 2020 ISA, primarily in the context for use in future ISAs, but to also provide some scientific advice for the second version of the draft PA for the reconsideration. It would be helpful to provide additional detail on the recent CASAC comments on the 2020 ISA review as part of the discussion on this topic (pages 1-15 and 1-16), including more detail on how that ISA feedback factored into the health effects chapter. In this draft PA there is only a single sentence on this issue (page 1-16, lines 6-9).

In the review completed in 2020 and this reconsideration, the Risk and Exposure Assessments (REAs) for health and welfare were included as appendices in the PA. It is not clear if this is the approach that the EPA will use for all NAAQS reviews going forward. In some cases, it may be inappropriate to make policy recommendations when questions on the REAs have not been fully discussed and addressed. This is especially true if there are significant updates or revisions to the REAs between the draft and final PA. Therefore, the CASAC recommends that the EPA adopt the traditional approach of evaluating the REAs as separate stand-alone documents prior to the release of the PA in future reviews.

Chapter 2 – Air Quality

1. To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?

Chapter 2 is clearly presented and provides useful context for the reconsideration. Chapter 2 repeats some information from the ISA and it is not clear that repetition is necessary unless it supports policy-relevant background information for the PA. Section 2.1 is a clear discussion of photochemistry and NOx-limited versus NOx-saturated regimes. Section 2.2 discusses sources and emissions of ozone precursors. The discussion of substantial uncertainty in volatile organic compound (VOC) inventories, especially from petrochemical activities, should be added to the last paragraph on page 2-5. The text should clearly state if methane (CH_4) is included or excluded from the VOC emissions discussed in this chapter. Ozone precursor emissions by sector in Figure 2-1 use source categories that differ from those in Appendix C. A common source sector naming convention or comparison table should be incorporated for cross comparison. Figure 2-1 should explain if biogenic CH_4 emissions are excluded from the pie chart or if they are included in the "Other" category. Wildfire, silviculture, and agricultural burning emissions in Figure 2-1 should also appear in the trend lines of Figure 2-2. Figures 2-3, 2-4, and 2-5 are extremely informative. In addition, it would be helpful to see additional county-level emission density maps for (1) CH_4, (2) biogenic VOCs, and (3) anthropogenic VOCs.

Section 2.3 presents ambient air monitoring and data handling conventions. Increasing the required ozone monitoring periods in states which are impacted by wildfires during early spring and late fall would provide valuable information on seasonal trends. Section 2.4 presents ozone in ambient air. In Section 2.4.2, the level of significance in the trends should be stated (p-value or equivalent). Figure 2-12 shows MDA8 ozone trends by region back to 2000. From this figure it appears that trends are downward in areas of the country where levels have been or are above the 70 ppb standard. However, the PA should note that there are areas in the west and the northeast that have not seen a downward trend in design values. In Figures 2-15 and 2-16 and the discussions on page 2-25 (lines 6-23), the text should clearly state if the MDA1 represents the single highest value across 2018-2020 or if it represents the three-year average of the single highest values in 2018, 2019, and 2020. Analysis of season-average ozone trends might be useful given the evidence from some studies that chronic ozone exposure may be a useful health and welfare metric (Jiang et al., 2023; Di et al., 2017).

Section 2.5 presents CMAQ chemical transport modeling with the zero-out approach to estimate U.S. background (USB), international, and natural contributions. The modeling methodology and model performance seem appropriate for this application. For additional clarity, the text in this section should clearly state if CO emissions were perturbed in simulations to determine the USB, and if not, then describe why they were not. It would be helpful to start this section with a short description of how USB is relevant for the decisions in setting the ozone NAAQS and EPA's motivation for the new analysis in this section. In Section 1.2, the legislative requirements are discussed including a summary of multiple court cases that involved the role of background concentrations in the setting of the NAAQS. The results of those court cases seem to provide contradictory information with regards to the role of background concentrations in the setting of the NAAQS. The EPA should clearly state if USB can be considered in the setting of NAAQS or if background concentrations are only considered in the implementation of the NAAQS. This will support the CASAC's ability to provide advice on USB.

Table 2-1 list ZFIRE (zero all fire emissions) as one of the model simulations; however, the results were not included in Chapter 2 or the Appendix. Also, this chapter should discuss the emissions inventories for India, global shipping, and global fire. Observations for global remote sites, along with the long-term trend analysis, can be compared to the CMAQ model estimates to provide a better perspective on USB. Section 2.5.1.6 should discuss methane changes since the Industrial Revolution, rather than using the term "Post-Industrial methane." Also, the discussion of uncertainty from methane emissions being a major limitation in understanding methane contributions to ozone is not accurate since global ambient methane concentrations are known through time by direct measurements and ice cores.

The figures and tables containing USB contribution on the average of the top 10 predicted ozone days and the 4th highest ozone days are very useful and relevant to policy decisions. They indicate that the West has higher predicted USB concentrations than the East, which includes higher contributions from international and natural sources. Within the West, high-elevation and near-border areas have particularly high USB which can reach concentrations close to the current level of the ozone standard (70 ppb) on specific days. Finally, it would be helpful to see a table in the appendix listing the USB (modeled concentration and biases adjusted concentration) at each individual ozone monitor in the U.S. on the top 10 predicted ozone days and the 4th highest ozone days. This would allow for a detailed USB analysis on a site-by-site basis.

Chapter 3 – Review of the Primary Standard

Overarching Comments

The CASAC finds that the PA summarizes a wide breadth of information and communicates well the EPA staff perspectives regarding the current ozone NAAQS. The 1100+ page document provides a wealth of material and considerations, bringing together policy-relevant discussions based upon data provided in the 2020 ISA and two subsequent staff reviews of studies published after the 2020 ISA assessment period (Luben et al., 2020; Duffney et al., 2022). A large amount of data was collected and analyzed for the ISA, however, the CASAC believes this wealth of information was not fully utilized in the PA. The staff's approach perspective did not appear to change with this reconsideration, and therefore the results are not different. All of the CASAC members,* except for one, are concerned that the approach taken in the PA may substantially underestimate public health risk.

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?

<u>Controlled Human Exposure Studies (CHEs)</u>

The presented rationale for relying on the CHE data is strong, but the exclusion of consideration of the epidemiological data is concerning. Although the CASAC acknowledges the uncertainties underlying

* This also includes all of the CASAC Ozone Panel members, except for the one CASAC member.

epidemiological studies, they have considerable strength and should be used to more realistically evaluate the adequacy of the current primary ozone standard. Moreover, the decision to exclude the epidemiological evidence from the risk assessment is puzzling given the strong statement on page 3-33, lines 8-14, which highlights that there are multiple studies with strong evidence linking ozone exposures with respiratory emergency department visits and hospital admissions. Since the NAAQS primary standard is for ozone and other photochemical oxidants, this merits the inclusion of epidemiological studies as they are not restricted to ozone exposure alone. While there is no scientific evidence that CHEs, as an independent line of evidence, are inherently more informative than epidemiological data, the reliance on CHEs in the PA prioritizes their value in informing the adequacy of the public health protection afforded by the ozone standard. The CASAC recommends that the presentation regarding CHEs and epidemiological studies be rebalanced to address the inherent limitations of CHEs in determining a lower bound for the level of the standard as well as to incorporate the information available from epidemiological studies.

<u>Application of risk estimates to children</u>

Extrapolating CHE studies with adult participants to apply to children requires a strong justification and more thorough explanation. Children are designated as an at-risk group due to substantial evidence that they are more sensitive to the adverse effects of ozone than adults. Risk is estimated in the PA for children "if the simulated children had the same sensitivity as the controlled human exposure study subjects" (page 3-79). However, the risk for children simulated to be more sensitive than the CHE study subjects was not explored. The absence of children from the reviewed CHE studies (and in the literature) is an "appreciable data limitation" and therefore, the use of CHE studies in risk estimation is limited.

<u>At-risk Populations</u>

At-risk populations are described at length in the Ozone ISA and children (especially children with asthma) and outdoor workers are identified as those with the most evidence of increased risk. While risks of children are estimated in the PA (see previous), those of outdoor workers are omitted due to "appreciable data limitations" (Page 3-66). This explanation is insufficient and ignoring this at-risk group may result in an underestimate of the public's adverse impacts. Estimation of the risk for at-risk populations may differ among various subpopulations (e.g., adults with asthma, outdoor workers) due to innate/acquired susceptibility, vulnerability tied to exposures, or a combination of both.

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

The approach taken in Chapter 3 of the PA, summarized in Fig 3-1, is consistent with that taken in the 2020 PA, and in the 2014 PA. The current draft PA responds to the CASAC's comments on the 2020 ISA on November 11, 2022, in part by expanding the justification for the approach. The risk estimates have been revised, updated, and improved, and the presentation is clear. The estimates are not substantially different from the 2020 PA.

The risk assessment continues to be driven by findings from the ozone CHE studies, especially those conducted at concentrations most relevant to the current standard, i.e., those at 80, 70, and 60 ppb, for 6.6 hr with prolonged exercise. The summary of respiratory effects from ozone exposures, based on CHE studies in the 2020 ISA, is accurate. These studies have shown effects on airway function and inflammation at concentrations as low as 60 ppb in healthy young adults (Kim et al., 2011). The PA acknowledges the limitations and uncertainties of this approach (Section 3.3.4), but justifies continued reliance on CHE data because they are the "most certain" (p. 3-7). The strong epidemiological evidence for short-term respiratory health effects is excluded from the risk analysis on the basis that the majority of studies were conducted in areas that would not have met the current standard. The stated concern is that health effects in those areas might have been driven by higher concentration distributions that would not have been experienced under conditions compliant with the standard. The CASAC finds that scientific evidence from some epidemiologic studies, e.g., studies that exclude days with high ambient concentrations or that estimate the concentration-response curve using a non-parametric smoother, do not support the EPA's assertion that the higher concentrations drive the risk estimate. Many studies that have evaluated this question find higher concentration-response estimates at lower concentrations.

The risk assessment focuses on people with asthma, with an appropriate emphasis on children with asthma. Because the CHE studies in healthy adults reviewed in the 2020 ISA have indicated that prolonged exposure with exercise is required to elicit airway effects at concentrations relevant to the standard, the children considered to be at risk are limited to those with moderate to heavy prolonged exercise outdoors.

The calculations, based on careful and clearly detailed estimations of ozone exposure and time activity levels, conclude that few children with asthma would be exposed more than once per year to 70 ppb for 7 hours at moderate to heavy exercise, under conditions that meet the current standards. The PA concludes (p. 3-115) that "…available evidence and exposure/risk information do not call into question the adequacy of protection provided by the existing standard or the scientific and public health judgments that informed the 2020 decision to retain the current standard…."

All of the CASAC members,* except for one, disagree with this conclusion, and find that the available evidence does call into question the adequacy of the protection provided by the current standard. The rationale and evidence for this finding are detailed below.

1. The PA fails to adequately consider and incorporate findings from epidemiological and panel studies of short-term respiratory effects in the exposure and risk analysis.

- Regardless of the design value for measured concentrations included in an epidemiological study, concentration-response (C-R) relationships at ambient concentrations below the regulatory standard can be informative. Epidemiological studies that have examined ozone exposure-response relationships provide evidence that exposures below 60 ppb are associated with health effects. An example is the exposure-response curve in Figure 3-8 from the 2020 ISA, taken from Strickland et al. (2010). Emergency Department (ED) visits in Atlanta for children with asthma were studied in relation to ozone exposures. As described on page 3-76 of the ISA, "Visual inspections of the plots revealed approximately linear associations and no evidence of a threshold with 8-hour daily max ozone concentrations as low as 30 ppb….” The bulk of the data, with the narrowest confidence intervals, are in the range of 45 to 65 ppb.

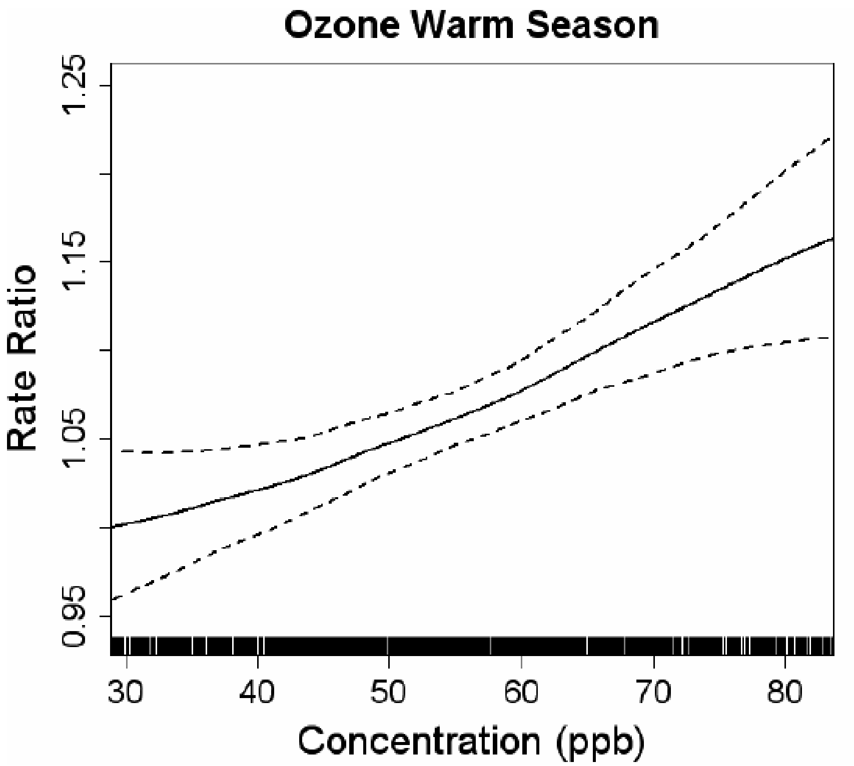

Figure 3-8 from the 2020 Ozone ISA. Locally estimated scatterplot smoothing (LOESS) C-R estimates and twice-standard-error estimates from generalized additive models for associations between 8-hour max 3-day avg ozone concentrations and emergency department (ED) visits for pediatric asthma. Strickland et al. (2010).

- Additional evidence to support health effects associations below the current standard is presented in the 2020 ISA, Figures 3-9, 3-10, and 3-11. These data contradict the contention that the findings in the epidemiological studies were somehow driven by the highest ozone concentrations.

- Also from the 2020 ISA, Table IS-4 summarizes evidence that short-term respiratory health effects are observed at lower ozone concentrations:

  “Evidence from many recent, large multicity epidemiological studies provide further support for an association between ozone and ED visits and hospital admissions for asthma; associations are generally strongest in magnitude for children between the ages of 5 and 18 years in studies with mean 8-h daily max ozone concentrations between 31 and 54 ppb. Additional epidemiological evidence for associations between ozone and hospital admissions

> and ED visits for combinations of respiratory diseases (31 to 50 ppb as the study mean 8-h daily max), ED visits for COPD (33 to 55 ppb as the study mean daily 1-h max), and ED visits for respiratory infection (33 to 55 ppb as the study mean daily 1-h max)."

- From the same table in the ISA:

> "Recent epidemiologic evidence for respiratory mortality is limited, but there remains evidence of consistent, positive associations, specifically in the summer months, with mean daily 8-h max ozone concentrations between 8.7 and 63 ppb. When recent evidence is considered in the context of the larger number of studies evaluated in the 2013 Ozone ISA, <u>there remains consistent evidence of an association between short-term ozone exposure and respiratory mortality</u>." [underline added]

- An additional key consideration from the epidemiological evidence is that a lower threshold for health effects either does not exist, or is below ambient concentrations in real-world settings.

- The Population, Exposure, Comparison, Outcome, and Study Design (PECOS) criteria in the ISA for study eligibility and consideration, excludes research from countries outside North America. For future reviews, the CASAC unanimously recommends that PECOS include consideration of health effects evidence from epidemiology and panel studies, and that the study selection criteria be broadened to include studies conducted outside of the U.S. and North America.

2. The exclusive reliance on CHE studies for the risk analysis is inappropriate, and underestimates the public health impacts for children, people with underlying lung disease including asthma, and other groups at increased risk.

- It is inappropriate to use findings from CHE studies to infer a lower level at which risk is minimal. The CASAC provided advice on this issue in its Report on the 2020 ISA on November 22, 2022:

> "The following summarizes the primary reasons why ozone CHE studies may underestimate or miss ozone effects at low concentrations: participants are not representative of the general population; exposures are usually to a single pollutant and of relatively short duration; exposures are to laboratory-generated ozone without other photochemical oxidants; and prior ambient pollutant exposures may affect the CHE ozone responses but are not typically characterized in CHE studies."

The PA does include a discussion of the limitations of CHEs, including the hazards of extrapolating findings in healthy adults to children with asthma. The PA acknowledges that children with asthma are at increased risk for adverse consequences from ozone exposure, with strong supporting evidence from studies of ED visits and hospital admissions for asthma, and correctly cites evidence that the developing respiratory tract may be especially at risk for airway remodeling effects and limitation of lung growth. It further concludes on page 3-30 that:

> "…consideration of differences in magnitude or severity, and also the relative transience or persistence of the responses (e.g., FEV_1 changes) and respiratory symptoms, as well as pre-existing sensitivity to effects on the respiratory system, and other factors, are important to characterizing implications for public health effects of an air pollutant such as O_3...."

Despite a thorough and important discussion in this section of the PA, this issue is subsequently relatively ignored, and is not incorporated into the risk assessment.

- It remains unclear whether people with asthma, or other underlying airways diseases, experience greater changes in lung function in response to ozone, compared with people without airways disease. As pointed out in the PA, CHE studies of people with generally mild, stable asthma have shown similar decrements in lung function as people without asthma. However, the studies on Mount Washington in the 1990s (Korrick et al., 1998) are relevant here. Day hikers on Mount Washington performed spirometry before and after their hike. Decrements in lung function were associated with ozone concentrations, and the association was robust to adjustment for $PM_{2.5}$ and aerosol acidity. The average of the hourly ozone concentrations during each hike ranged from 21 to 74 ppb, and the concentration-response relationship for FEV_1 and FVC indicated linear decrements between 40 and 70 ppb. Of note, hikers with a history of asthma or wheeze showed a fourfold greater decrease in FEV_1 in association with ozone than hikers without such a history. The findings suggest that people with airways disease may experience substantially greater ozone-related effects with ambient exposures, compared with the CHE setting, and that effects are occurring below the current standard.

- The risk assessment considers, based on the CHE data available in 2020, that moderate to heavy exercise for multiple hours is necessary in order to elicit decrements in lung function at ozone concentrations relevant to the standard. However, in 2020, there were no studies with participants exposed to ozone for 6.6 hours *at rest*, to confirm the absence of effects. Such a study has now been published (Hernandez et al., 2021). Fourteen healthy young adults (without asthma) underwent resting exposures to 70 ppb ozone, or clean air, for 6.6 hours. FEV_1 decreased 2.8% relative to clean air control exposures, with evidence for increased airway inflammation. From Figure 2, panel B of that paper, it appears that 3 of 14 subjects had differential decreases in FEV_1 of about 10%, indicating effects were not negligible for all participants. The study calls into question the assumption that moderate to heavy exercise is necessary for adverse health effects. It has important implications for the risk assessment. The estimates of the number of people with asthma with exposures of concern will need to be expanded to include resting exposures. The APEX exposure modeling will need to be modified to include all 7-hour benchmark exposures, regardless of exertion level. This indicates the current standard is not adequately protective for people with asthma and other respiratory diseases who are spending time outdoors, even without exercise.

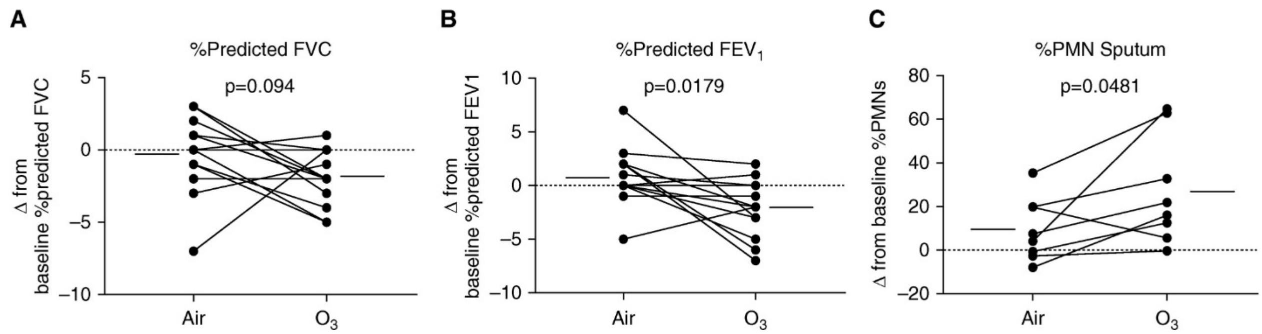

Figure 2. (A and B) Change from preexposure % predicted FVC (A) and FEV_1 (B) after 6.6-hour exposure to clean air (CA) or an average O_3 concentration of 70 ppb (n = 14). (C) Change from preexposure sputum PMNs of the O_3 and CA exposures (n = 8 paired sputum samples of sufficient quality for analyses). Horizontal bars in A–C denote the mean. O_3 = ozone; PMN = neutrophils (Hernandez et al., 2021).

All of the CASAC members,* except for one, therefore conclude that the exclusive use of findings from CHE studies to determine a minimal-risk lower exposure level is inappropriate, especially given the absence of CHE data in children with asthma. As summarized above and in the 2020 ISA, there is convincing evidence from the epidemiological studies that children with asthma are being adversely affected at concentrations below the current standard. The overreliance on CHE data to establish a no-effect threshold, and to estimate numbers of people with exposures of concern, combined with complete exclusion of the epidemiological findings in the risk analysis, leads to a serious underestimation of the public health risk associated with exposures under the current ozone standard. The Administrator's considerations regarding the ozone standard will be best served by considering a fuller range of plausible possibilities, based on all relevant data.

However, one CASAC member agrees with the PA's conclusion that the available evidence and exposure/risk information do not call into question the adequacy of protection provided by the existing standard and that the current primary ozone standard should be retained without revision. Relying on information provided in the PA, this member believes that the results of the scientific evidence (e.g., epidemiological studies and human exposure studies) must be evaluated in the proper context of the standard to determine the adequacy of a standard. In other words, all elements of the standard (indicator, averaging time, form, and level) and the way attainment with the standard is determined (i.e., highest design value in the Core Based Statistical Area [CBSA]) must be considered when determining the appropriate level for the standard. This is important because setting standards based on the highest design value in the CBSA results in a spatial concentration distribution across the CBSA that is assumed to provide adequate protection at concentrations well below the level of the standard. The most common way to do this analysis is to perform a risk and exposure assessment to determine the spatial concentration distributions that individuals are exposed to in a study area and the resulting risk at the current and alternative standards. There were no epidemiological studies conducted in U.S. locations with ambient air ozone concentrations that would meet the current standard for the entire duration of the study. However, epidemiological studies that were conducted in study areas with design values near the standard of 70 ppb could provide useful information. Unfortunately, a risk and exposure assessment using C-R functions from epidemiological studies was not conducted; therefore, the PA is limited in its ability to use epidemiological studies to provide insights regarding health outcomes that might be expected under air quality conditions that meet the current and alternative standards. Accordingly, the studies of 6.6-hour exposures with quasi-continuous exercise, and particularly those for concentrations ranging from 60 to 80 ppb, are the focus in this reconsideration. At a standard of 70 ppb, the REA estimates that: (1) more than 99.9% of children with asthma are protected from a single exposure during moderate to heavy exercise at/above 80 ppb and 100% are protected from multiple exposures, (2) more than 99% of children with asthma are protected from a single such exposure at/above 70 ppb and more than 99.9% are protected from experiencing multiple exposures, and (3) more than 95% of children with asthma are protected from experiencing multiple such exposures at/above 60 ppb. This member believes that this demonstrates that under the assumptions made in the PA, the current standard will provide adequate protection at concentrations well below the level of the standard. The scientific evidence and quantitative exposure and risk information on which this reconsideration is based are largely unchanged since the NAAQS reviews that ended in 2015 and 2020. In the 2015 NAAQS decision, the Administrator concluded that a primary ozone standard of 70 ppb was requisite to protect public health with an adequate margin of safety. The current draft PA's conclusion to retain the current standard of 70 ppb is at the upper bound of the range of 60 – 70 ppb recommended by the CASAC in their review of the 2014 PA. In the 2020 PA, the EPA concluded that the current primary ozone standard of 70 ppb should be retained without revision and the majority of CASAC members agreed with this in their review of the 2020 PA.

The other CASAC members note that this member's comments did not address their concerns and comments regarding the PA and REA, which are detailed above. Most notably, these members find that it is inappropriate to use findings from CHE studies to infer a lower level at which risk is minimal. The CHE study results do not directly translate to sensitive subgroups such as children with asthma. Furthermore, new evidence has emerged that lung function decrements, increased symptoms, and airway inflammation occur even without exercise, which substantially increases the estimated number of individuals with exposures of concern. The overreliance on CHE data to establish a no-effect threshold, and to estimate numbers of people with exposures of concern, combined with the complete exclusion of the epidemiological findings in the risk analysis, leads to a serious underestimation of the public health risk associated with exposures under the current ozone standard.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

Greater reliance on and interrogation of the epidemiological data in the REA. The CASAC strongly believes that the preponderance of epidemiological findings related to ozone's short-term respiratory health effects was not adequately used in preparing the current PA. Despite the uncertainties associated with potential co-pollutant confounding and assessing NAAQS-relevant design values for cities where the epidemiological studies were conducted, the CASAC encourages the EPA to consider alternative and novel approaches for analyzing historic population-based epidemiological data. These approaches could include using truncated distributions or observations censored to include days below the benchmark concentrations, meta- or combined-analyses, and advanced methods for disaggregating the shape of concentration-response (C-R) curve at parts of the exposure distribution more relevant to the NAAQS benchmark level.

The CASAC believes that this is consistent with recommendations from the 2022 NASEM report, "Advancing the Framework for Assessing Causality of Health and Welfare Effects to Inform National Ambient Air Quality Standard Reviews" urging the EPA to look into emerging research methods, which include advanced methods for controlling for confounding, the use of novel causal inference techniques, joint effects modeling, and the application of untargeted, highly-multidimensional data in making causal inference through machine learning methods.

Examining alternative forms of the ozone standard in the PA. The CASAC recommends that the form of the current ozone standard be reevaluated in future reviews. The CASAC has concerns about the form's statistical robustness, stability, and the general arbitrariness (i.e., non-scientific rationale) of selecting the fourth highest day. The CASAC suggests:

- Assessing the impact of having a seasonal (i.e., 6-month or warm-month) long-term form in addition to the current daily form. This would be similar to daily and long-term forms for the $PM_{2.5}$ NAAQS. Since the peak to mean ozone ratio is highly variable across locations, areas with lower ratios (i.e., fewer MDA8 high values but chronically elevated concentrations typical of more rural areas away from large urban areas) might require a different form of a NAAQS to provide protection similar to other, largely urban, locales.
- Examining and comparing the current design values with values based on integrated concentrations. For example, a 10 highest day mean may be more statistically stable, while providing greater protection from extreme concentrations than allowed by the current form.

Additional research needs. There are several gaps in the current ozone health effects literature the committee identified, including:

- The need for **more controlled human studies** of mild, stable, people with asthma who are at rest. The CASAC acknowledges the importance of relying on studies such as Hernandez et al. (2021) and stressed the need for validating findings involving ozone exposures at benchmark levels and in extending them to people with asthma.
- **Consideration of health effects of ozone mixtures and joint effects.** The CASAC suggests looking beyond traditional independent ozone health effects, given the potential joint, synergistic, or priming effects of ozone exposure occurring within a complex mixture. There is a need for future health effect studies to examine ozone exposures in the presence of other co-pollutants, including other atmospheric oxidants. The CASAC acknowledges the methodological difficulty of multipollutant assessments, but sees opportunities, in both: a) controlled human exposure designs; and b) panel studies, as examples for future studies to investigate short-term effects of ozone. In addition, considering mixtures and/or joint effects in cohort studies would better inform inference about health effects from chronic exposures or developmental effects of exposures during sensitive periods such as pregnancy or early life.

- **Monitoring technology improvements.** Lower cost monitoring technologies for ozone remain fairly uncertain, particularly for measurements in ambient concentration ranges. If these technologies are to be useful in future epidemiological studies, it is likely necessary to improve these technologies to reduce their uncertainty and improve their accuracy.
- **Panel studies.** Beyond potentially serving as a means of assessing ozone effects in multipollutant exposure settings, the CASAC acknowledges the need to promote additional research involving panels and small cohorts of: a) participants spending time outdoors and b) including other, non-respiratory endpoints (e.g., cardiovascular effects similar to those measured in the MOSES2 study). These designs will become increasingly central to understanding ozone health impacts, particularly among sensitive subpopulations and/or when ambient exposures are observed near or below benchmark concentrations.

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary standard?

The PA provides detailed analyses of various welfare effects and the rationales for determining their levels of causality. These in turn are used to evaluate the efficacy of these measures for determining ozone exposures that would provide the requisite protection of the public welfare. The CASAC finds that the PA provides excellent reviews of the degrees of causality for vegetation, ecosystems, and plant-insect interaction responses to ozone, but that the discussion of its influences on climate could be clarified and strengthened.

The PA review of the secondary standard was divided into six thematic sections: (1) a historical overview of the process used to set the current secondary standard, (2) a summary of the available and *newly* available scientific evidence for ozone impacts on vegetation and ecosystems, (3) a description of the various effects that could constitute public welfare effects, (4) supporting quantitative air quality and exposure analyses, (5) key considerations and recommendations regarding the secondary standard, and (6) a discussion of uncertainties and limitations in the scientific assessment.

The PA begins with a largely historical discussion of the benefits of having a single season cumulative secondary standard, as recommended by previous CASAC reviews, versus a 3-year cumulative index. The PA describes the process by which the Administrator at the time noted that to keep the median relative biomass loss (RBL) for trees at 6% or lower required a single year W126 exposure index of 19 ppm-hrs, but that if a 3-year average was to be used, it should be lowered to 17 ppm-hrs, as the CASAC recommended at that time. Based on the evidence at that time, doing so would virtually eliminate exposures that could result in a 6% or greater median RBL. Specifically, the PA on p. 4-6 states: "… and accordingly, to eliminate or virtually eliminate cumulative exposures associated with a median RBL of 6% or greater." The PA notes also that the Administrator determined that it would be appropriate to consider additional metrics, particularly the number of hours or days with ozone ≥ 100 ppb.

The PA then reviews the various ozone effects across levels of organization, from plants to ecosystems. These include visible foliar injury, biomass and yield losses for trees and crops, respectively, plant-insect interactions, and ecosystem processes such as productivity, hydrology, biogeochemical cycling, and community composition. It concludes with a discussion of the effects of tropospheric ozone on climate. The PA emphasizes that those effects having the strongest evidence (i.e., determined to be causal), such as RBL in tree seedlings and relative yield loss (RYL) for crops, are most useful for setting the secondary standard, and serve as proxy for “consideration of the broader array of related vegetation-related effects of potential public welfare significance” (p. 4-5), although some in this category, such as visible foliar injury, may not be as useful for reasons described below. Effects that have been determined to be “likely to be causal” help elucidate potential ozone impacts but may not be useful in determining a protective level of the secondary standard because of either a scarcity of studies or higher degrees of uncertainty in the conclusions, because “the tools for quantitative estimates were more uncertain” (p. 4-5). The PA thoroughly addresses the types of ozone impacts that could affect or are relevant to public welfare and includes considerable discussion about whether these ozone impacts could be used to support these conclusions.

The CASAC notes that summary conclusions from past CASAC reviews regarding RBL for trees were derived prior to the publication of Lee et al. (2022), which enlarged the pool of species analyzed from 11 to 16 and implemented a considerably improved approach by subjecting all suitable studies (i.e., those meeting criteria for data completeness and experimental design) to a common statistical analysis that used a Weibull function to regress biomass against a standardized 92-day cumulative W126 exposure index. Furthermore, the Lee et al. (2022) study included 95% confidence levels for the exposure-response relationships, considered whether single-year exposures could be cumulated over multiple years, and whether there were effects due to diurnal and seasonal patterns of ozone concentrations. In this new study, the tree species analyzed collectively spanned a wide range of sensitivities and covered large geographical areas of the United States. Species ranked “most sensitive” exhibited RBLs of 5% at W126 values ranging from 2.5 to 9.2 ppm-hrs. These values are considerably lower than those considered by the previous CASAC, which were identified as limiting the *median* RBL to 6%.

Figures 4D-3 to 4D-5 show the relationships between the accumulated 92-day W126 index and the 4th highest daily maximum 8-hr average of ozone concentrations. At the current secondary standard of 70 ppb, there are numerous sites exceeding a W126 index of 9 ppm-hrs, totaling 77 (or 7%) of U.S. monitoring sites for 2018-2020 (Table 4D-3). Most, if not all, of these sites are for trees in the West and Southwest, with a few also in the West North Carolina region. At a W126 index of 9 ppm-hrs, this would rise to 245 sites and from Table 4D-6, there are 159 sites that exceed both the current secondary standard and a W126 of 9 ppm-hrs. Combined with the information above highlighting that sensitive trees have greater than 5% RBL above a W126 of 9 ppm-hrs, this information illustrates that there are a larger number of sites (159) where trees are not adequately protected by the current secondary standard.

The CASAC recommends that more discussion is needed regarding ozone impacts on RYL in agricultural crops. Given recent publications demonstrating significant RYL from ozone for soybean, wheat, maize, and rice (Tai et al., 2021; Mills et al., 2018), the adequacy of an exposure index derived from either a 7- or 8-hr ozone average warrants further discussion, particularly with reference to the implications for public welfare and the ability to protect against detriments in crop protection and food security.

The CASAC agrees with the EPA that tropospheric ozone effects on climate should not, at this time, be used to set a secondary standard because of the difficulty in relating ground-level concentrations to U.S. or global climate effects. However, the CASAC suggests that the arguments developed by the EPA regarding tropospheric ozone effects on climate could be more clearly laid out. The uncertainties highlighted on page 4-63 – 4-64 differ from the uncertainties that are given as the reason for discounting the influence of ozone on climate discussed in Section 4.5.2. Later, on page 4-119, the EPA provides additional explanations for excluding the effects of tropospheric ozone on climate. The CASAC suggests that these difference in justification be clarified across sections in the PA and that the EPA consider including a broader discussion of factors for why it would be difficult to establish an ozone standard that protects against the damages of climate change. (See Dr. Jason West's individual comments for further details.)

The CASAC also finds that a discussion of the effects of ozone precursor emissions (NOx, VOCs, CO and CH_4) on climate would enhance the EPA's discussion of ozone impacts. How ozone is reduced affects climate impacts in addition to ozone concentration levels, and discussion of this could strengthen the EPA's arguments for not currently recommending a secondary standard for ozone effects on climate.

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?

Visible foliar injury, derived primarily from USFS Biomonitoring Sites, and extensively discussed throughout the PA, was not deemed sufficiently useful for setting the secondary standard, due to an inability to generalize across regions and species, and because many studies were not designed to allow a determination of the impacts on public welfare. In addition, direct links between visible foliar injury and alterations in growth and physiology are difficult to establish. Thus, this parameter, although "causally" related to ozone exposure, was deemed not as useful for standard setting as either the RBL for trees or the RYL for crops, where relationships between ozone exposure and public welfare are stronger. Therefore, the CASAC agrees with the EPA that visible foliar injury should not be used at this time as a scientific justification for setting the secondary standard.

The CASAC agrees with the conclusions of the EPA that tropospheric ozone can affect insect-plant interactions. These include (1) alterations in feeding and pollinator behavior, caused by changes in plant biochemistry upon exposure to ozone, (2) oxidative reactions that alter volatiles that pollinators use for long-distance location of flowers, and (3) alterations in plant signaling that affect plant responses to herbivores and/or their predators. The CASAC also agrees with the EPA that there are currently too few studies in this area of inquiry and that uncertainties among and between studies reduce confidence in their usefulness for determining if the secondary standard should be changed.

The methodologies employed to determine the exposure-response functions as described in Lee and Hogsett (1996), Lee et al., (2022), as well as the resultant uncertainties are well explained (e.g., p. 4-54) and the CASAC is confident of the technical and statistical rigor employed. The CASAC also shares concerns with the EPA about whether single-year exposure-response functions can be extrapolated to multiple years. Few studies have followed tree exposures for multiple years and trees grown in pots instead of in the ground can become root-bound, as Lee et al. (2022) note, and this may influence responses in later years. However, these authors did mention that biomass responses at the ASPEN-FACE site, where aspen trees grown in the ground rather than in pots were exposed to ozone over 6 years had consistent exposure-response functions with 1-year studies of aspen seedlings, and the EPA concurred that a 1-year function was adequate to describe effects in subsequent years. However, the EPA cautioned that such a conclusion is based on very few studies. The CASAC concludes that further study is desirable before exposure-response relationships from multi-year exposure studies can be used with confidence in the standard setting process.

There is also uncertainty associated with extrapolating impacts on seedlings/saplings to large, mature trees, something that has been discussed by researchers many times in the past, but for which there are few technical solutions and few funding opportunities to conduct such studies because of the costs involved. The CASAC has confidence in the exposure-response analyses done on tree seedlings and also concludes that more efforts should be made to extrapolate beyond seedling studies to account for potential ontogenetic changes in responses to ozone.

Discussion of community-level effects should include alterations in competitive relationships among species due to differential sensitivity of species to ozone (Barbo et al., 2002). The CASAC also notes that there is little information on ozone responses in other types of vegetation, such as perennial grasses, which are common to the Great Plains and cover large geographical areas of the Midwest.

There is extensive discussion in the PA about agricultural practices that could alter responses of crops to ozone. The PA concludes that this makes it difficult to assess the relevance of some RYL functions for the standard setting procedure. The PA does mention some agricultural practices such as irrigation and fertilization, that could affect responses to ozone, but it does not expand on the mechanisms responsible. Nor does it consider the economic impacts of those practices that moderate responses to ozone, which because of the additional expenses involved, could be viewed as detrimental to public welfare. The NCLAN (National Crop Loss Assessment Network) studied ozone responses of major crops that covered over 70% of U.S. farmland and were the most complete and informative such studies up to that point in time (Heck et al., 1988). The CASAC recommends that the EPA make more explicit references to how these agricultural practices modify responses to ozone in ways that have consequences for setting the secondary standard. In addition, the EPA should also take into consideration more recent studies showing causal relationships between ozone and crop yields (Mills et al., 2018; Tai et al., 2021).

2. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

In the PA, the EPA concludes that the scientific evidence and quantitative air quality and exposure analyses support retention of the current standard, without revision. All of the CASAC members,* except for one, find that section 4.5 does not provide appropriate and sufficient rationale to support this conclusion with respect to the current secondary standard.

Specifically, these CASAC members find that the current secondary standard does not provide sufficient protection against the public welfare effects of air pollution. For visible foliar injury, the PA demonstrates that while not deemed sufficiently useful for setting the secondary standard, the current standard is expected to result in lower severity and incidence of visible foliar injury, and, by extension, reduced impacts on aesthetic and recreational values. The current standard does not, however, provide sufficient protection against reduced growth effects in sensitive tree species and ecosystems, annual plants, and in crops of major importance to U.S. food security. While the EPA finds that at 17 ppm-hrs, the median response of the combined studies results in a relative biomass loss (RBL) of less than 6%, the nonlinearity of the exposure-response relationship calls into question the application of the median value to draw this conclusion. Additionally, EPA's recommendation for the 3-year averaging time is based on analysis of RBL and did not include relative yield loss (RYL) of annual plants, including agricultural crops.

At a W126 index value of 17 ppm-hrs, the most recent data (Lee et al., 2022) show that nearly half (i.e., seven) of the 16 tree species for which exposure-response functions exist – species with a broad range throughout the U.S. that are assumed to represent the range of ozone sensitivity for species without exposure-response functions (page 4-60) – experience a RBL ranging from 9-29% (page 4A-34), an effect that is compounded over time in long-lived species, such as trees. For annual crops, a W126 index value of 17 ppm-hrs results in RYL ranging from 6-12% for five of 10 crop species (page 4A-17). Among these are three of the most important U.S. crops in terms of cash crop receipts (i.e., cotton, soybean, winter wheat). Because nearly half of species studied would be significantly affected at a W126 index value of 17 ppm-hrs, and because impacts on many other species remain unknown, these CASAC members do not find this level to be protective.

All of the CASAC members,* except for one, recommend a W126 index value of 7-9 ppm-hrs as the target level of protection, such that RBL and RYL are ≤5% for the majority (>69%) of species. At 9 ppm-hrs, 69% (11 out of 16) of tree species (page 4A-34) and 100% of annual crop species (page 4A-19) with exposure-response relationships experience ≤5% RBL and RYL, respectively. At 7 and 8 ppm-hrs, >75% of tree species and 100% of annual crop species experience ≤5% RBL and RYL, respectively. The recommendation for trees is based on the more recent peer-reviewed Lee et al. (2022) publication rather than the older Lee and Hogsett (1996) report because: (1) an expanded number of species were included in Lee et al. (2022); (2) in both studies, the results are similar for most tree species. At 9 ppm-hrs, Lee and Hogsett (1996) found that 90% of the tree species (10 out of 11) experience ≤5% RBL (page A4-19). Ponderosa pine and tulip poplar RBLs reported by Lee et al. (2022) were 5.5% and 12.2% (page 4A-34), higher than the respective 3.2% and 2.6% (page 4A-16) RBLs reported for these species in Lee and Hogsett (1996); and (3) Lee et al. (2022) includes an improved methodological approach that was peer-reviewed, whereas the Lee and Hogsett (1996) findings were not peer-reviewed. The statistical approach in Lee et al. (2022) was standardized for all species (e.g., a 92-day period was employed). In addition, a covariate for initial tree seedling size was included in the models.

For the averaging time, these CASAC members suggest that the W126 be accumulated over a rolling 92-day window, and that the highest value be considered. With regards to the form, these CASAC members recommend a single year highest cumulative W126 index value not to be exceeded more than 2 years out of any 5-year interval. This accounts for interannual variability yet ensures that the target W126 index value is met in more years than not.

In addition to protecting against public welfare effects associated with reduced growth in sensitive tree species and annual crops, this recommended secondary standard is also expected to control for the effects of peak concentrations on plant growth. EPA analyses (Table 4-1) show that with an annual W126 index value ≤15 ppm-hrs, only 9% of monitoring sites during the 2018-2020 period experience more than zero hours with ozone concentrations >100 ppb per year (N100 > 0), and 1.2% sites experience more than five hours with such high ozone values (N100 > 5). At a W126 index value ≤7 ppm-hrs, ~5% and 0.4% of sites experience more than zero and more than five hours over 100 ppb, respectively. Data on the occurrence of peak concentrations are not available for the W126 index value of 9 ppm-hrs that is at the upper end of the level of the secondary standard proposed here, but presumably, at this level, sites would experience peak concentration occurrences closer to those for a W126 index value of 7 ppm-hrs.

These CASAC members' recommendation for implementing a secondary standard is comparable to an earlier 2014 CASAC recommendation "that the level associated with this form be within the range of 7 ppm-hrs to 15 ppm-hrs to protect against current and anticipated welfare effects of ozone." This recommendation is also comparable to recommendations by the National Park Service (NPS) to use a lower benchmark value similar to that used by NPS, which describes 7 ppm-hrs to 13 ppm-hrs as "moderate conditions" for vegetation health. Finally, the recommendation is also consistent with the Lee et al. (2022) study that estimates a maximum of 9.2 ppm-hrs would protect sensitive species at a 5% RBL level.

Regarding EPA's conclusions on potential alternative options to the current secondary standard, all CASAC members agree with the EPA that it is important to consider both a cumulative exposure metric and a peak exposure metric in assessing the air quality conditions that would be protective of public welfare effects of ozone impacts on vegetation.

However, one CASAC member, relying on the information presented in the PA, supports the EPA staff preliminary conclusion that the body of evidence and the quantitative air quality and exposure analyses do not call into question the adequacy of the protection provided by the current secondary standard and the current secondary ozone standard should be retained without revision. The remainder of this paragraph provides this CASAC member's rationale for supporting this conclusion. According to Table 4A-11, a median (RBL) of 6.0% is associated with a W126 index between 23 and 24 ppm-hrs and a median RBL of 2.9% is associated with a W126 index of 17 ppm-hrs. The PA states (page 4-102), "The evidence does not indicate single-year seasonal exposure in combination with the established E-R functions to be a better predictor of RBL than a seasonal exposure based on a multiyear average. Accordingly, it is reasonable to conclude that the evidence provides support for use of a multiyear average in assessing the level of protection provided by the current standard from cumulative seasonal exposures related to RBL of concern based on the established E-R functions." In addition, the use of a three-year average seasonal W126 index provides stability to the standard by recognizing that there is year-to-year variability in environmental factors (e.g., rainfall and meteorological factors) that influence the magnitude and distribution of ozone in any year. Figure 4-12 contains a scatter plot of W126 (3-year average and annual values) versus 8-hour ozone design values based on 2018-2020 data. It shows that the seasonal W126 index values (3-year average) are at or below 17 ppm-hrs when the current standard is met at all 877 monitoring locations that were examined. Also, over 99% of single-year W126 values were at or below 19 ppm-hrs. The form and averaging time of the standard are not required to match those of the exposure metrics, as long as the standard, in all its elements, provides requisite protection against effects characterized for exposures of concern. Therefore, this member agrees with the arguments presented by the EPA in the PA that the current 8-hour ozone standard can be used as a surrogate for the W126 exposure metric. In addition, this member believes that any recommendation for an alternative secondary standard should be evaluated in the proper context of the standard to determine the adequacy of the alternative standard. In other words, given this perspective, all elements of the standard (indicator, averaging time, form, and level) and the way attainment with the standard is determined (i.e., highest design value in the CBSA) be considered when determining the appropriate level for the standard. This member believes that setting standards based on the highest design value in the CBSA results in a spatial concentration distribution across the CBSA that is assumed to provide adequate protection at concentrations well below the level of the standard. Without this additional analysis, it is difficult to determine the adequacy of any alternative secondary standards. This CASAC member finds that the scientific body of evidence and the quantitative air quality and exposure analyses on which this reconsideration is based are largely unchanged since the 2015 and 2020 ozone NAAQS decisions. This member agrees with the Administrator's decision in 2015 that a secondary ozone standard of 70 ppb was requisite to protect the public welfare from any known or anticipated adverse effects as well as the 2020 decision to retain the secondary standard of 70 ppb without revision.

The other CASAC members note that this member's comments did not address their concerns and comments regarding the PA, which are detailed above. Most notably, these CASAC members find that the median value should not be used to determine whether the current standard is adequate given the nonlinearity of the RBL function. These members also find that the current scientific evidence indicates that the current standard provides insufficient protection against reduced growth effects on sensitive tree species, ecosystems, annual plants, and crops of major importance to U.S. food security.

For climate impacts of ozone, the CASAC finds that there is strong evidence that anthropogenic climate change is occurring, that elevated concentrations of ozone are important for global climate, and that emissions from the U.S. are contributing to that warming. However, the CASAC agrees with the EPA that it is not straightforward to relate concentrations of ozone at ground level with climate changes from ozone, and as such, the CASAC agrees that the basis is insufficient to support a secondary standard for ozone based on impacts on climate.

3. What are the Panel's views regarding the areas for additional research identified in section 4.6? Are there additional areas that should be highlighted?

The CASAC finds that the additional research areas discussed in the Policy Assessment are comprehensive and well presented. Additional areas for research include:

- Extending exposure-response functions to ecosystem-level effects and determining subsequent welfare implications;
- Further studies on whether single-year exposure-response functions can be extrapolated to multiple years;
- Further studies of the viability of extrapolating ozone impacts on seedlings/saplings to large, mature trees to account for potential ontogenetic changes in response to ozone;
- Better understanding the effect of climate change as a factor modifying the relationship between ozone and vegetation;
- The impact of ozone on climate and on quantitative tools to relate ground-level concentrations with ozone radiative forcing and climate changes;
- More data on how ozone influences different vegetation types (including not just trees but also grasses, forbs, etc.) and plants across different life stages, and species from various functional groups;
- Agricultural crops merit additional focus in ozone research to better inform the secondary standard, especially those aspects of crop management that may exacerbate or mitigate ozone effects on crops;
- The CASAC agrees with the EPA that it is critical to consider the role of peak concentrations in assessing the air quality conditions that would be protective of public welfare effects of ozone impacts on vegetation. Thus, additional research into the role of peak concentrations (e.g., varying thresholds) on plant health is recommended.

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Appendix A

Individual Comments by the 2022 CASAC Ozone Review Panel Members on the *Policy Assessment (PA) for the Reconsideration of the Ozone National Ambient Air Quality Standards (External Review Draft Version 2)*

Mr. George A. Allen

Chapter 1 – Introduction

1. To what extent does the Panel find that the information in Chapter 1 is clearly presented and provides useful context for this reconsideration?

Chapter 1 provides an overview of the Policy Assessment Document, describing the purpose, legislative requirements, history of the O3 NAAQS, the 2020 review of the O3 NAAQS, and the rationale for this reconsideration. Of note for Chapter 2, the introduction states that the ambient air monitoring data has been updated since the 2020 PA. Overall, this chapter provides a clear and useful background and context for the revised PA reconsideration document.

Sections 1.1 and 1.2 clearly describe the Purpose and Legislative Requirements for the PA and NAAQS review, noting that CASAC advice on any revision to the standards is provided as part of the PA review. The Clean Air Act sections that govern NAAQS revisions and subsequent court decisions that refine the requirements of a NAAQS review are clearly described and referenced here and in Section 1.3. The CASAC advisory functions in its charter are listed, noting that some of those functions are not relevant to standard settings but may be with regard to implementation.

Section 1.3 is a detailed history of the O3 NAAQS, including NAAQS reviews and decisions going back to the first Total Photochemical Oxidants standard set in 1970 and noting the many changes in indicator, level, and form that have occurred in reviews since then. It notes that this reconsideration is not the first for O3; the 2010 CASAC reconsideration of the 2008 decision was completed but not implemented by the administration. The various court decisions regarding EPA's setting of the secondary O3 NAAQS are also documented. Understanding the history of the O3 NAAQS reviews over the last twenty years is important for putting the current review in proper context, and this section presents a useful and complete summary of that history.

Sections 1.4 (summary of the 2020 review) and 1.5, this reconsideration of the 2020 O3 NAAQS Decision, clearly provide the rationale for this reconsideration: the divergence from past practices including limitations of the down-sized and expedited process for the previous review and the lack of an expert Panel to augment CASAC member expertise. Section 1.5 notes EPA's provisional assessment memos from 2020 and 2022 as the basis for not reopening the 2020 air quality criteria review (the ISA), and briefly describes the CASAC unsolicited discussion of the 2020 ISA last fall (2022). While that discussion did not result in a recommendation that the 2020 ISA be reopened or revised, the CASAC did express concerns regarding some aspects of the 2020 ISA primarily in the context for use in future ISAs but to also provide some scientific advice for a reconsidered PA. It would be helpful to provide additional detail on the CASAC comments from the 2020 ISA review as part of this discussion on pages

1-15 and 1-16 of this chapter, including how that feedback factored into the health effects chapter of this revised reconsidered PA.

Chapter 2 – Air Quality

1. To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?

Section 2.1 is a clear discussion of photochemistry and NOx limited vs. saturated regimes as a function of distance from sources. In Section 2.2 the discussion of substantial uncertainty (usually under-estimation) in VOC inventories (NEI, especially from petrochemical activities) could benefit from additional discussion (page 2-5, lines 9-11) since as NOx emissions are better controlled we move closer to VOC-limited conditions and control strategies.

Figure 2-12 shows MDA8 (regulatory) O3 trends by region back to 2000. From this figure it appears that trends are downward in areas of the country where levels have been or are above the 70 ppb standard. That is sometimes not the case since about 2010 in areas like the west and the northeast; an example is the design value trend for the metro NYC domain (NY-NJ-CT), with no trend since 2009, now in severe non-attainment with the 70 ppb NAAQS:
https://portal.ct.gov/-/media/DEEP/air_monitoring/trends/CT-Ozone-Design-Value-Trends.jpg
In areas such as this where reductions are most needed, achieving attainment may be very difficult with current control strategies. The PA could state this clearly, since that is not the message from the trend plots.

Analysis of season-average O3 trends might be useful given the evidence from some studies that chronic O3 exposure may be a useful health (and welfare) metric. (European Heart Journal reference below and Di et al., NEJM 2017).

Figure 12-13d (Mt. Washington NH) diurnal pattern is a good example of high-elevation O3 lacking any notable diel cycle.

The summary of background O3 in section 2.5 is useful, even though it might not be considered in setting a NAAQS; there are court decisions on this cited in chapter 1 that appear contradictory. It may be worth noting here that there have been different definitions of background O3; the 2013 ISA reported and analyzed both North American (NAB) and USB. Now it is just US anthropogenic sources that are zero'd out in the modeling of background O3.

The discussion of wildfire contribution to O3 in section 2.5.1.3 on page 2-33 notes that it can be from a mix of "natural" and anthropogenic sources when a plume passes over an urban area, adding NOx emissions. It is unclear how this is handled in models of USB, or if it is a factor worth considering in the context of non-US emissions; Section 2.5.2.2, page 2-41, notes that model performance for O3 from wildfires is historically poor. In the context of DV calculations, it is my understanding that EPA exceptional event guidance allows state and local air agencies to exclude all of an exceedance day when it can be demonstrated that wildfire plumes made any contribution to the observed O3 MDA8 value. In other words, if the EE demonstration shows there was a likely contribution (not quantified) of any wildfire O3 to an exceedance event, the day is discarded instead of being counted as an exceedance event for use in DV calculations. There was a discussion with Ben Wells of OAQPS staff and me on this at the meeting where he said this was not how it worked, but in my sidebar with him after that discussion he said that the updated guidance might allow the entire day to be set aside for DV calculations; this is what was done by the State of CT's EE demonstration for the Ft. McMurray fires on May 25-29, 2016. With wildfire smoke now being relatively common, perhaps this approach should be reconsidered. A very recent example that may trigger EE submissions in the midwest and northeast US is the April 14, 2023 transported wildfire smoke plume that appears to have caused a wide swath of exceedances. It should be noted that gas-phase elemental mercury could be present in wildfire smoke from areas with historical mercury deposition to soil, and that this is a strong positive interference with the UV-photometry method that is widely used in the ambient O3 monitoring networks.

Section 2.5.3.3 is a good discussion of how background O3 can vary as a function of total O3.

Chapter 3 – Review of the Primary Standard

Additional Comments, Health Effects

Evidence for cardiovascular effects

The references below from the European Heart Journal (March 2023) look at cardiovascular hospital admissions, not mortality - that might be an important distinction from other epi studies on O3 health effects. Jiang et al, "Ozone pollution and hospital admissions for cardiovascular events":
https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehad091/7070974
and related editorial "The emergence of the air pollutant ozone as a significant cardiovascular killer?":
https://academic.oup.com/eurheartj/advance-article/doi/10.1093/eurheartj/ehad046/7070973
(The 10 ug/m3 increment O3 metric used here is 5 ppb)
It is a well done study and analysis done in China. N was large, 6.5 million hospital admissions. They ran several 2-pollutant models [Table 2], which even for PM2.5 didn't change most of the outcome effects. The main analysis was MDA8, but they also used 24-h average O3 and saw stronger effects for some outcomes; the O3 diel cycle there [average MDA8 vs. 24-h concentrations in Table 1] may not be as strong as we see here in urban areas. Temperature was included as a covariate. The discussion section and Section 5 of the Supplemental Material is very useful - a mini lit review.

It was done in China (Andrea Baccarelli, Columbia Mailman SPH is an author). Would PECOS exclude it? This paper should probably be on the provisional assessment list for EPA to look at before a final rule is issued.

Wright et al. (March 2023, https://ehjournal.biomedcentral.com/articles/10.1186/s12940-023-00978-9) from folks at Oxford, done in China. O3 was associated with CVD and stroke after adjustment for other pollutants. As before, would PECOS exclude this?

A 2022 Toyib et al. study (https://journals.lww.com/epidem/Fulltext/2022/11000/Long_term_Exposure_to_Oxidant_Gases_and_Mortality_.2.aspx) showed stronger associations between O3 and mortality in areas where the oxidative potential of PM2.5 was higher. This could explain why the O3 mortality association is not consistent across studies.

Other 2022 studies showing associations with O3 and cardiovascular indicators or mortality:
Niu et al., https://www.sciencedirect.com/science/article/pii/S2542519622000936
Liu et al., https://www.sciencedirect.com/science/article/pii/S0160412022002070
Zong et al., https://www.mdpi.com/1660-4601/19/18/11186

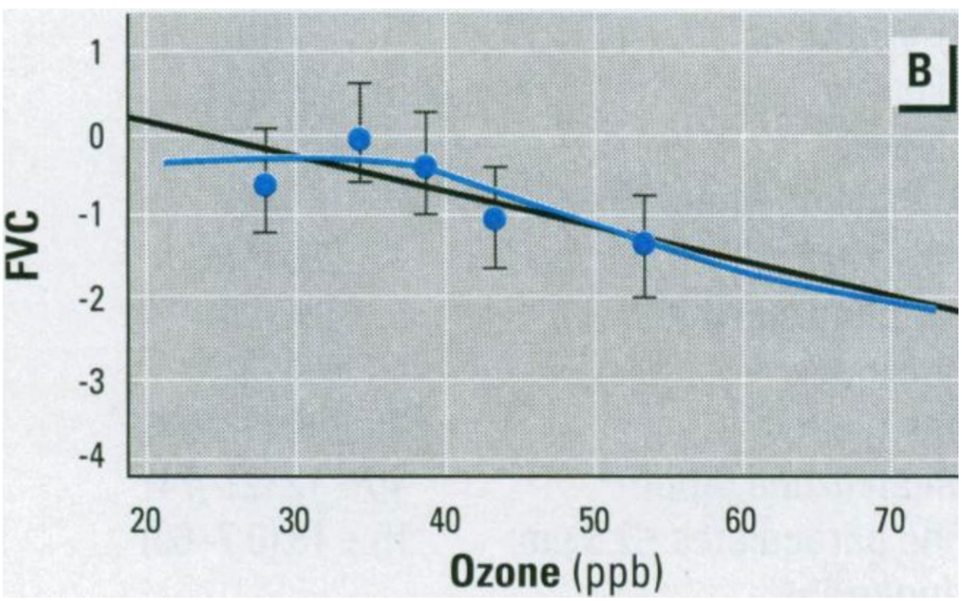
As with Jiang and Wright above, these were done in China, but might be excluded by PECOS? Does the PECOS geographic exclusion criteria need to be revised to not automatically exclude these studies in the next review?

I remain concerned, as noted in my ISA comments last fall, that EPA's reviews of study quality does not sufficiently scrutinize long-term mortality epi studies that report hazard ratios well below 1.0 as shown in Figure 6-8 of the 2020 ISA. It is implausible that O3 is good for you, as these results suggest, and confounding by co-occurring pollutants that are inversely associated with O3 and not properly controlled for is the likely cause, as noted by Hvidtfeldt et al. 2019 (https://www.sciencedirect.com/science/article/pii/S016041201831969X) and Stafoggia et al. 2022 (the ELAPSE study, https://www.sciencedirect.com/science/article/pii/S2542519621002771). This issue should be explicitly addressed in the next ISA.

Limitations of controlled human exposure studies

EPA is relying primarily on controlled human exposure (CHE) studies in this PA. While they are useful for some health endpoints like airway inflammation, CASAC has previously noted the substantial limitations of these studies for quantifying O3 health effects. They use only O3, not the mix of O3 and related photo-chemical oxidants found in ambient air. We tend to forget that while O3 is the regulatory indicator, the NAAQS is for O3 and related photochemical oxidants - there's a reason for that definition. CHE studies assume there is no effect, especially no cardio-vascular effect, of the related photochemical oxidants. We don't have anything to support that assumption, and there are epi studies that suggest that the O3 "mix" in ambient air has effects that are not observed in O3 only exposures, especially cardio-vascular effects. CHE study subjects are often young and healthy, and certainly not elderly with significant pre-existing disease. Thus the results generally do not reflect the adverse effects of the CHE O3 concentrations to sensitive population sub-groups.

A study of more than 500 subjects outdoors hiking Mt. Washington, NH (Korrick et al., EHP 1998, https://ehp.niehs.nih.gov/doi/abs/10.1289/ehp.9810693) had a subset [n=40] of participants with asthma or a history of wheeze. Even though exposures were mostly well below 70 and even 60 and 50 ppb, there was a 4x larger decrement in FEV1 or FVC pre/post hike compared to no asthma/wheeze diagnoses. This could be useful in the context of interpreting CHE study effects on sensitive subgroups. Effects were observed below 50 ppb [Figure 1 below]; the exposure for the top quintile was 53 ppb. This work isn't cited in the PA or the ISA for this round of reviews, but is in the 2013 ISA.



The April 6, 2023 public comment letter from Drs. Thurston and Harkema makes it clear that the ATS/ERS 2017 joint ERS/ATS policy statement on what constitutes an adverse health effect of air pollution states that in asthmatics these kinds of modest decrements in lung function (as observed in Korrick et al. above) are considered to be an adverse effect, even without accompanying respiratory symptoms:

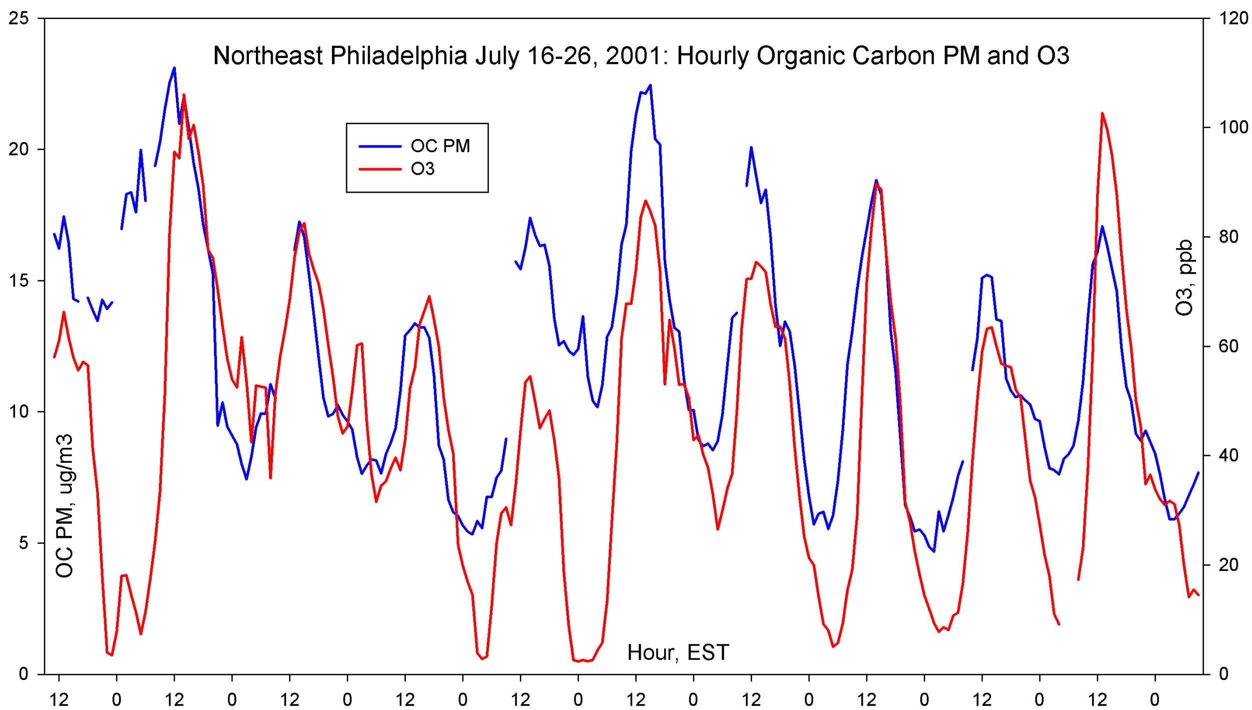
"… while small transient reductions in lung functions in healthy adults should not be considered an adverse health effect, similar lung function changes in vulnerable populations, including individuals with existing respiratory disease such as asthma should be considered an adverse health effect."

A very recent publication (since the March meeting) shows that "that exposure to modest postnatal O3 concentrations increases risk of asthma and wheeze among the vulnerable subpopulation of infants experiencing bronchiolitis." Dearborn, et al. in https://journals.lww.com/epidem/Abstract/9900/Role_of_air_pollution_in_development_of_asthma.132.aspx . This, along with the Korrick study above are examples of adverse effects at levels below the current O3 NAAQS. Other recent literature that should be included in any provisional assessment prior to a final rule, in addition to the cites above, include: https://ehp.niehs.nih.gov/doi/10.1289/EHP11661

These studies, in addition to the ones referenced in the reconsidered PA, demonstrate that short-term respiratory adverse effects occur at levels below the current NAAQS, and demonstrate the need for a more protective standard for vulnerable populations.

A correction to my ISA individual comments from October 2022

In my ISA comments I included a plot of O3 and organic carbon PM from 2001 showing a strong diel association between O3 and OC that could be part of why we observe cardiovascular effects from ambient O3 exposures but not from controlled exposure studies. That plot had errors in the x-axis time-scale, and a corrected version is shown below.



Mr. Ed Avol

Chapter 3 – Review of the Primary Standard

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?

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

General Overview

I commend EPA staff for their diligent and impressive efforts in assembling the 2020 Version Two Policy Assessment (PA). The PA summarizes a wide breadth of information and communicates EPA staff perspectives regarding the current O3 NAAQS. The 1100+ page document provides a wealth of material and considerations, bringing together policy-relevant discussions based upon data provided in the 2020 Integrated Science Assessment (ISA) and two subsequent staff reviews of studies published after the 2020 ISA assessment period (Luben et al 2020, Duffney et al 2022).

In my opinion however, the policy judgements reached in the Version Two Draft PA present the message that the current standard is sufficiently protective, and I do not believe that to be the case. I suggest that the approach and determinations made by staff in the PA leading to the judgements reached are occasionally misinformed and lead to several misinterpretations. There are also several areas of future research needs that are worthy of consideration. Addressing these would strengthen this review and subsequent future documents, better leverage the strengths of the existing publication data base, provide targeted motivation for possible future research directions and funding efforts to close existing informational data gaps, and better serve the Administrator as he seeks to make a determination of an "adequate margin of safety".

I respectfully differ with the PA's conclusion that the existing data base supports the retention of the current standard, because I believe several data elements have been under-valued (particularly with regard to epidemiological studies in general, studies conducted in other countries, and the multiple organ systems in which human health changes have been documented) to the point that there does not exist a "margin of safety" in the current ozone NAAQS. Since the 2015 review, additional research studies and data released support and strengthen concerns about a broader array of systemic health outcomes. The history of health standards setting has generally been one of additional emerging data leading to an almost uni-directional strengthening of existing standards to account for more subtle dysfunctional changes identified through more sophisticated research efforts. In my view, the totality of sub-clinical findings affecting multiple organ systems and/or multiple endpoints has not been appropriately "weighted", resulting in acceptance of the existing ozone NAAQS rather than supporting tightening of the standard. The 2020 ISA itself speaks to the totality of findings when it states (in the ISA Executive Summary, ES 5.1):

> An inherent strength of the evidence integration in this ISA is the extensive amount (in both breadth and depth) of available evidence resulting from decades of scientific research that describes the relationship between both short- and long-term ozone exposure and health effects. The breadth of the enormous database is illustrated by the different scientific disciplines that provide evidence (e.g., controlled human exposure, epidemiologic, animal toxicological studies), the range of health outcomes examined (e.g., respiratory, cardiovascular, metabolic, reproductive, and nervous system effects, cancer and mortality), and the large number of studies within several of these outcome categories. The depth of the literature base is exemplified by the examination of effects that range from biomarkers of exposure, to subclinical effects, to overt clinical effects, and even mortality.

In the case of the ozone NAAQS and its several cycles of reviews, we have witnessed iterative changes in the standard from one hour of exposure to multiple hours, acknowledging the cumulative impacts on human health. We have witnessed the tightening of the level of the standard as additional information became available at lower levels of exposure. We have witnessed additional health endpoints become subjects of scrutiny and concern, as health researchers have identified additional organ systems or cellular processes that responded in negative fashion to the challenge of persistent low-level exposures. Decades ago, respiratory-related outcomes – followed by cardiovascular outcomes - were the main areas for health concerns and regulatory action. With improved tools and mechanistic understanding, we currently consider respiratory, cardiovascular, neurologic, metabolic, reproductive, and cellular changes at increasingly lower levels of exposure. Based on research across multiple organ systems, I suggest there is cumulative evidence of damage that should raise concerns about the adequacy of the current standard.

Providing the Administrator with a factual basis for his deliberations regarding an *adequate* margin of safety is a worthy and valued objective of these collective CASAC efforts. In my opinion however, the PA document in its current form under-emphasizes the impacts of ozone on human health by:

(1) 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);
(2) utilizing a literature base that is too narrowly construed, because the PECOS criteria for study eligibility and consideration exclude research from countries outside North America (in other words, ozone exposures and research studies of appropriate quality and documentation do exist outside of North America!);
(3) placing disproportionate emphasis on findings from clinical exposure studies as reported in the ISA (since volunteers for chamber studies ethically and appropriately do not include the most at-risk or sensitive individuals from the larger population [such as those with more serious chronic disease or young children or from communities of color or with multiple concurrent intrinsic or extrinsic health risk factors], findings from chamber studies may be important indicators of health endpoints of potential concern but likely under-report the true severity of response to exposure in the population-at-large (and in my opinion, represent "the tip of the iceberg" in identifying health outcomes of concern among populations of interest).

I suggest that the presented evidence in the ISA and PA provide a measure for health-based discussion but not a "minimal-effects" threshold for regulation. I believe that the presented data collectively lays a foundation for the Administrator to consider a revised ozone NAAQS more stringent that the current NAAQS of 70 ppb.

The PA document 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.

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.

Broader actual consideration of "at-risk" groups would also benefit the document and better serve consideration of public health impacts. While children with asthma are indeed at increased risk based on the available data, other population segments with co-existing intrinsic or extrinsic susceptibility factors also merit attention. These include (but may not be limited to): *adults* with asthma or other diseases such as diabetes, obesity, and chronic obstructive pulmonary disease (COPD); segments of the population with co-existing considerations such as poor-quality housing, inadequate health care, or certain genetic dispositions; *outdoor workers* (who are often people of color dealing with other additional vulnerability factors, including pre-existing disease or poor-quality housing or inadequate health care); in our current society, multiple concurrent factors can unfortunately "add up" and impose a substantive cumulative burden on sensitive subsets of the population. I am concerned that such a strong emphasis on children with asthma may have pre-empted consideration of other possible susceptible sub-groups. I strongly encourage an effort to identify any existing data on these other sub-groups and future investigation into their potential at-risk status.

More Specific Chapter 3 Comments

1) **(an observation regarding word choice …)**
[Several places, including] P121 line17 (middle of p3-25) and P134, line35 (bottom of p3-38) – "…respiratory responses to short-term exposures as the most *sensitive* effects of O3." I suggest the phrase "*most sensitive*" be re-considered, and changed to "most robust", "most convincing", "most compelling", "strongest", or "most commonly observed". Most clinicians would likely consider lung function testing (and possibly patient-reported symptoms) as relatively "blunt" response endpoints compared to assorted blood markers, cardiologic assessments, neurologic indicators, or metabolic indices. Respiratory measurements are understandably the most widely used given the expected route of entry to the body by airborne toxicants, but something about the phrase "*most sensitive*" seems slightly off-the-mark. In my opinion, the perspective is better-captured in line 3 of p123 (top of p 3-27) which states that "the *strongest* evidence of O3-related effects continues to document the respiratory effects of O3…".

2) **P131 (bottom of p3-35, just prior to Table 3.1)** In the context of policy, there is discussion of age groups of asthma sensitivity and a focus on children. It is noted that children are a high-risk group (spending more time outdoors, being at increased risk while organ systems are developing, being naïve to undertake protective behaviors, …). It is further noted that asthma is higher in girls than boys among 5-19yr olds. The text goes on to note that additional factors such as EJ and SES tend to increase potential risk status for children with asthma.

   Looking at the issue more widely, asthma has another prevalence "bump" later in life (sometimes denoted as "adult-onset" or "late-onset" asthma). This has been observed both among former childhood asthmatics whose symptoms "disappeared" in their teen years but resurfaced in their 20s. 30s. 40s, or even later in life, as well as the apparent development of asthma later in life with no apparent pediatric history. Interestingly later in life, asthma prevalence seems to reverse and is higher in boys than girls. Accordingly, another at-risk group might be 40/50/60+ men and women, who are outdoor workers (for example, construction, farmworkers, oil/gas extraction, utility, postal service, truck/port/rail/commercial yard warehousing, …) . Layer onto the age range and occupation susceptibilities the observation that many in this group are also people of color or limited SES, and the potential risk status of this sub-population further increases. My point is that from a *policy* perspective, thinking about at-risk groups through the lens of multiple layers of specific risk factors can be informative. In my opinion, as currently presented, that broader policy perspective of multi-layered risk factors combining to change the risk status for sub-groups in the population seems more muted in this section in lieu of a "spotlight" focus on children with asthma. From a policy standpoint, children should not be the "only" population sub-group of concern.

3) **P162 (last para of p3-66, lines26-28)** – As in previous exposure assessments, the identification of outdoor workers as an at-risk group is made but not included in any analyses due to "appreciable data limitations". As Footnote #74 (bottom of P162 [p3-66] describes, exploratory analyses estimated a larger portion of this sub-group would be exposed than the populations considered in the analyses. The apparent concern is dismissed by noting that comparative results from the 2014 health risk assessment suggested that fewer people would have been exposed to benchmark concentrations. This recurring identification but ultimate dismissal of an identifiably at-risk population is an area for future research needs, given the size and characteristics of the identified group. Consideration should be given to addressing this recurring shortfall as soon as possible to obtain the needed information and be positioned to objectively assess the potential for exposure and risk in a near-future cycle of evaluation.

4) **P206 (first para, p3-110)** – The justification for focusing exposure and risk analyses on children is arguably somewhat circular and self-fulfilling. It is noted that there are more adults in the US with asthma and that outdoor workers (a substantive number of whom have other concurrent health conditions such as asthma, obesity, cardiovascular disease, or diabetes) are at potential increased risk, but since exposure and health estimates for those workers are uncertain, few or no estimates are provided in the PA, and their at-risk status is not considered in regulatory determinations. Protecting children, especially those with compromised respiratory health, is undeniably of great importance, but the cyclical repetition of acknowledging and then discarding consideration of other identified at-risk groups due to uncertainties is a recurring gap to be addressed. If identified groups have a credible basis for consideration but relevant data is lacking, prioritized efforts should be undertaken to fill identified information gaps through targeted research funding in future data collection cycles.

5) **P211 (bottom of p3-115) Section 3.6 Key Uncertainties and Areas for Future Research**

A need for multi-pollutant exposure consideration – With each successive cycle of CASAC review, more subtle and insightful consideration of exposure complexities and health interactions are addressed. However, the reality of multi-pollutant exposures continues to be ignored. Ambient exposures do not occur one toxicant at a time, and we should not continue to consider pollutant impacts one at a time. The PA document notes that the relative risk of identifiable sub-groups can be markedly affected by intrinsic and extrinsic factors such as health status, genetic traits, race/ethnicity, occupation, SES, etc., and researchers strive to adjust these factors into analytical approaches for more accurate and appropriate assessments. In an analogous manner, it should be acknowledged that real-world NOx and SOx exposure effects can involve both gas and particle-phase components of the atmospheric nitrates or sulfates present, and that ambient ozone exposures do not occur in the complete absence of other airborne contaminants. In the near-term, improved statistical methodological approaches have helped and can continue to help address these realities, but co-exposure or successive exposure events DO occur in the real world, can affect human response, and need to be factored into the Administrator's determination of "an adequate margin of safety". I suggest that just as SES or race or occupation is considered as an additional factor that elevates potential health risk, co-exposures should also be considered in this same manner. There are several published studies on the impacts of co-exposure, so there already is a literature to consider and build upon.

Comment on a more balanced consideration of data from clinical, epidemiological, and toxicological studies - Clinical (chamber) studies are valued for their single-pollutant exposure approach and discrete assessment of specific exposure effects, but ambient (multi-pollutant) pre-exposure prior to purposeful chamber exposures, post-exposure follow-up durations and protocols, ethical concerns that restrict health status of volunteers participating in clinical studies, the representativeness of the actual study population, the age range of participants participating in most clinical studies, and other related observations limit interpretation of the generalizability of chamber exposure research.

This approach serves a valued purpose – providing specificity of exposure-response relationships but should be viewed in a broader data collection context. Epidemiology (e.g., community research of real-world exposures with participants going about their daily activities) provides relevancy (if not the discrete specificity of clinical studies). Animal toxicology and lab-bench studies provide critically important mechanistic and cell pathology insights. Collectively, these should be considered as "a three-legged stool", with each leg providing important balance and contributions, and future research support should reflect that multi-pronged appreciation and approach rather than the down-weighting of one approach to the emphasis on another.

Community-based data gaps - Epidemiological research provides real-world relevance but also introduces exposure misclassification and unavoidable multipollutant exposures. In addition to identifying outdoor workers as a group of exposure and health concern, usable information is apparently not sufficiently available to support improved understanding of: (1) the exposures in this large and varied group of generally adults; (2) incorporation of outdoor workers' activity patterns (hours of work at increased levels of ventilation and heart rate in various locations proximal to concurrent toxicant exposures); (3) observable health impacts in the face of co-existing health status (such as adult-onset asthma, high-blood pressure, obesity, or diabetes). Given the size, breadth, and variability of this at-risk population, data collection efforts should be strategized and supported to obtain this information.

Limited low-exposure studies among populations of interest – As noted in the PA, identification of free-living populations at or below concentrations of regulatory interest (in the case of ozone, below 70ppb for 8 hours or more) was challenging. Multi-pollutant confounding makes data collection, analyses, and interpretation difficult as well. Nevertheless, obtaining this information is important in both clinical exposure studies and in community-based investigations, to confirm/validate apparent findings in either research domain.

Improved exposure assessment – The advent of low-cost sensors and community science to crowd-source or obtain information at geographically greater precision than previously available has revolutionized PM research. Improvements in credible low-cost ozone sensors hold promise to do the same for ozone exposure and health assessments and should be pursued.

Dr. James Boylan

Balanced CASAC

Based on the 2020 PM and ozone reviews and the recent PM and current ozone reconsideration reviews, it is clear that the previous and current CASAC lack a proper balance of scientific perspectives. I would like to emphasize the importance of keeping a balanced set of perspectives on the chartered CASAC and the panel members. Since the chartered CASAC and panel members are appointed, the “majority” and “minority” opinions can be directly determined by those selections.

The topics for discussion in the CASAC deliberations are complex and there usually is not a clear right or wrong answer. The CAA does not require the standard to be set at zero risk. Therefore, multiple lines of evidence and associated uncertainty must be evaluated and weighed to come to a determination of what is an acceptable risk when determining if the current standards are adequate or need to be lowered.

In the 2020 PM review, the chartered CASAC consisted of one consultant, four state/local air pollution control agency representatives, and one research professor. The seventh CASAC member resigned during the deliberations. In the 2020 CASAC recommendations, five CASAC members supported retaining the current annual $PM_{2.5}$ NAAQS while only one member supported lowering it; and all six CASAC members unanimously supported retaining the current daily $PM_{2.5}$ NAAQS. In the most recent PM review, the chartered CASAC consisted of one state air pollution control agency representative and six research professors. In the 2022 CASAC recommendations, all seven CASAC members unanimously supported lowering the current annual $PM_{2.5}$ NAAQS (however, they could not agree on the range); and six CASAC members supported lowering the current daily $PM_{2.5}$ NAAQS while only one member supported retaining it. The science did not change between these two reviews, but the “majority” and “minority” opinions drastically changed simply based on who was appointed to the CASAC.

In the 2020 ozone review, the chartered CASAC consisted of one consultant, four state/local air pollution control agency representatives, and two research professors. In the 2020 CASAC recommendations, six CASAC members supported retaining the current primary ozone NAAQS while only one member supported lowering it; and all seven CASAC members unanimously supported retaining the current secondary ozone NAAQS. In the current ozone reconsideration review, the chartered CASAC consists of one state air pollution control agency representative and six research professors. In the current CASAC recommendations, six CASAC members supported lowering the current primary ozone NAAQS while only one member supported retaining it; and six CASAC members supported lowering the current secondary ozone NAAQS while only one member supported retaining it. The science did not change between these two reviews, but the “majority” and “minority” opinions drastically changed simply based on who was appointed to the CASAC.

In all these reviews, the CASAC members consisted of highly creditable nationally recognized scientists, but the CASAC was clearly unbalanced in perspectives. In an unbalanced CASAC, the recommendation of the minority should not be dismissed, especially if the minority recommendations are directly supported by evidence presented in the ISA and PA documents.

An April 12, 2023 InsideEPA.com article titled "EPA Defends CASAC Membership In Suit Brought By Former Panel Chair" quotes EPA as saying "In particular, the Administrator is not required (and did not try) to make appointments to the Committee based on predications about what position each of the 100 candidates would likely take on the many scientific issues regarding air quality that come before the Committee." However, I feel that EPA should make a conscious decision to appoint CASAC members and panel members with a balance of positions and broad perspectives from a variety of backgrounds, including additional representatives from state/local air pollution control agencies and industry. While it is nice to try to achieve unanimous consensus, it is even more important to include a fair balance of scientific viewpoints so that the Administrator can make an unbiased and informed decision on the adequacy of the standards.

Chapter 1 – Introduction

To what extent does the Panel find that the information in Chapter 1 is clearly presented and provides useful context for this reconsideration?

The information in Chapter 1 is clearly presented and provides useful content for this reconsideration. The information on the history of the ozone NAAQS reviews and decisions was well done and especially useful. In the review completed in 2020 and this reconsideration, the Risk and Exposure Assessments (REAs) for health and welfare were included as appendices in the PA. It is not clear if this is the approach EPA will use for all NAAQS reviews going forward. In some cases, it may be inappropriate to make policy recommendations when questions on the REAs have not been fully discussed and addressed. This is especially true if there are significant updates or revisions to the REAs between the draft and final PA. Therefore, the traditional approach of evaluating the REAs as separate stand-alone documents prior to the release of the PA seems more appropriate.

Chapter 2 – Air Quality

To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?
Chapter 2 is clearly presented and provides useful context for the reconsideration.

Technically, CH_4 is a VOC; however, many times CH_4 is excluded from VOC emissions. It is not clear if CH_4 is included in the VOC emissions or not. The text should clearly state if CH_4 is included or excluded from the VOC emissions discussed in this Chapter.

Figures 2-3, 2-4, and 2-5 are very helpful to see the spatial distribution of CO, NOx, and VOC emissions. In addition, it would be helpful to see additional county-level emission density maps for (1) CH_4 since it is one of the four primary precursors of tropospheric ozone, (2) biogenic VOCs, and (3) anthropogenic VOCs.

On page 2-25, "MDA1" is defined on lines 3-4 as the "daily maximum 1-hour average" concentrations. Lines 6-7 state, "Figure 2-15 shows boxplots of MDA1 values at U.S. monitoring sites based on 2018-2020 data stratified by each site's 8-hour O3 design value." It is not clear if the MDA1 represents the single highest value across 2018-2020 or if it represents the three-year average of the single highest values in 2018, 2019, and 2020. Please clarify. Also, the y-axis in Figure 2-15 is labeled as "Daily Maximum 1-hour O3 Concentration (ppb)". To make it consistent with the MDA1 definition in lines 3-4, it appears that "average" should be added to the label to read "Daily Maximum 1-hour Average O3 Concentration (ppb)". On page 2-25 (lines 10-11), "160" should be changed to "180" and "the rightmost bin" should be changed to "the two rightmost bins" to read "…there is an increasing presence of higher MDA1 values extending up to around 180 ppb for the two rightmost bins which includes only sites that exceed the current standards."

Section 2.5 presents CMAQ chemical transport modeling with the zero-out approach to estimate U.S. background (USB), international, and natural contributions. The modeling methodology and model performance seem appropriate for this application. Table 2-1 list ZFIRE (zero all fire emissions) as one of the simulations. However, I did not see this information presented in this chapter or the Appendix. I would recommend adding ZFIRE to the Appendix. The figures and tables containing USB contribution on the average of the top 10 predicted O_3 days and the 4th highest O_3 days are very useful and relevant to policy decisions. They indicate that the West has higher predicted USB concentrations than the East, which includes higher contributions from international and natural sources. Within the West, high-elevation and near-border areas have particularly high USB which can reach concentrations close to the current level of the ozone standard (70 ppb) on specific days. These findings are consistent with the findings in the peer reviewed literature (e.g., Fiore et al., 2014 and Guo et al., 2018). Finally, it would be helpful to see a table in the Appendix listing the USB (modeled concentration and biases adjusted concentration) at each individual ozone monitor in the U.S. on the top 10 predicted O_3 days and the 4th highest O_3 day. This would allow analysis on a site-by-site basis.

Chapter 3 – Review of the Primary Standard

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?

The approach to considering the health effects evidence and the risk assessment to inform preliminary conclusions on the primary standard is sound and reasonable. There were no epidemiologic studies conducted in U.S. locations with ambient air ozone concentrations that would meet the current standard for the entire duration of the study. However, epidemiologic studies that were conducted in study areas with design values near the standard of 70 ppb could provide useful information. Unfortunately, a risk and exposure assessment using concentration-response functions from epidemiologic studies was not conducted; therefore, epidemiologic studies are limited in their ability to provide insights regarding health outcomes that might be expected under air quality conditions that meet the current and alternative standards. Accordingly, the studies of 6.6-hour exposures with quasi-continuous exercise, and particularly those for concentrations ranging from 60 to 80 ppb, are the focus in this reconsideration.

The risk assessment methodology seems appropriate for this application. For the risk assessment, hourly census-tract level ozone concentrations just meeting air quality scenarios (65, 70, 75 ppb) were developed for eight urban study areas using 2016 CAMx photochemical modeling with HDDM, 2015-2017 hourly ozone concentrations at individual monitors, and Voronoi Neighbor Averaging (VNA) interpolation. The hourly census-tract level ozone concentrations were used as inputs to the Air Pollutants Exposure Model (APEX). APEX uses the hourly air quality surface in each study area, along with U.S. census tract population demographics, to estimate the number of days per year each simulated individual in a particular study area experiences a daily maximum 7-hour average ozone exposure at or above benchmark levels of 60, 70, and 80 ppb. In addition, the number and percent of individuals expected to experience a lung function decrement (FEV_1 reductions of 10%, 15%, and 20%) in each study area were estimated using an exposure-response function derived from controlled human exposure study data.

The "# of sites" shown in Figure 3C-25 for Atlanta in January is "14". However, Georgia only has one or two year-round monitors in the state. Please check the "# of sites" in January for the other urban study areas. Table 3C-19 containing percent emissions changes used for each urban area to just meet each of the 24 air quality scenarios evaluated should include a negative (-) sign to indicate emission reductions.

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

The results of the scientific evidence (e.g., epidemiologic studies and human exposure studies) must be evaluated in the proper context of the standard to determine the adequacy of a standard. In other words, all elements of the standard (indicator, averaging time, form, and level) and the way attainment with the standard is determined (i.e., highest design value in the CBSA) must be considered when determining the appropriate level for the standard. This is important because setting standards based on the highest design value in the CBSA results in a spatial concentration distribution across the CBSA that provides adequate protection at concentrations well below the level of the standard. The most common way to do this analysis is to perform a risk and exposure assessment to determine the spatial concentration distributions that individuals are exposed to in a study area and the resulting risk at the current and alternative standards. At a standard of 70 ppb, the 189-page REA estimates that: (1) more than 99.9% of children with asthma are protected from even a single exposure at/above 80 ppb and 100% are protected from multiple exposures, (2) more than 99% of children with asthma are protected from even a single exposure at/above 70 ppb and more than 99.9% are protected from experiencing multiple exposures, and (3) more than 95% of children with asthma are protected from experiencing multiple exposures at/above 60 ppb. This demonstrates that the current standard will provide adequate protection at concentrations well below the level of the standard.

Based on the information provided in the PA, including the detailed REA, and the discussion provided in Section 3.5, I support the EPA staff preliminary conclusion that the available evidence and exposure/risk information do not call into question the adequacy of protection provided by the existing standard and the current primary ozone standard should be retained without revision. The scientific evidence and quantitative exposure and risk information on which this reconsideration is based are largely unchanged since the 2015 and 2020 reviews. In the 2015 and 2020 reviews, the Administrator concluded that a primary ozone standard of 70 ppb was requisite to protect public health with an adequate margin of safety. In addition, this conclusion is consistent with the recommendation from the 2014 CASAC that included 70 ppb in the range supported by scientific evidence and the 2020 CASAC where all but one member supported EPA's conclusion that the current primary ozone standard should be retained without revision.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

Page 3-7 (lines 1-2) states "Advice from the CASAC did not raise objections with the indicator, averaging time and form of the existing standard (Cox, 2020)." However, the 2020 CASAC response to the charge question on future research recommended "Further research into the form of the ozone standard with specific focus on moving from the fourth-highest daily maximum 8-hour ozone concentrations to a more integrated approach (e.g. average of 10 highest daily maximum 8-hour ozone average concentrations.)" The evaluation of alternative forms of the standard was not possible in the review completed in 2020 or the current reconsideration due to time limitations. However, in the next full ozone review, alternative forms of the standard should be investigated.

The current form of the standard is discussed in Section 3.1 (page 3-6). For the previous three ozone standards, the form has been the annual fourth-highest daily maximum 8-hour ozone average concentration, averaged over 3 years. The PA discusses the findings that this form better represents the continuum of health effects associated with increasing ozone concentrations compared to the exceedance form of the previous 1-hour ozone standard. Consideration was given to the fifth-highest value and the use of a percentile-based form. In addition, it was recognized that this form of the standard provides stability with regard to implementation of the standard. However, the PA does not discuss the possible use of an "integrated" form of the standard (e.g., average of 10 highest daily maximum 8-hour ozone average concentrations).

Conceptually, an "integrated" form of the standard should provide a better representation of the continuum of health effects associated with increasing ozone concentrations. Typically, the higher end of the daily maximum 8-hour ozone average concentration distribution drives health effects. The current form of the standard throws away the three highest concentrations (which typically would have the most significant health impacts) and ignores other potentially high concentrations beyond the fourth-highest daily maximum 8-hour ozone average concentration. This means that the entire ozone season is characterized by a single 8-hour average ozone measurement. As a result, a monitor that measures three high ozone values (e.g., 105, 101, 99 ppb) and the fourth-high value of 70 ppb would have the same fourth-high value as another monitor which measures 70 ppb for each of its four highest concentrations. In addition, the current form of the standard ignores the remainder of the higher end of the daily maximum 8-hour ozone average concentration distribution (i.e., fifth-high, sixth-high, seventh-high, eighth-high, ninth-high, and tenth-high). An integrated form of the standard (e.g., 10-day average) would be able to better account for these higher concentrations as part of a multi-day average of daily maximum 8-hour ozone average concentrations. In addition, an integrated form of the standard would provide greater stability than the current form of the standard with regard to implementation of the standard.

In the next full ozone review, EPA should compare the current form of the standard against various integrated forms of the standard to determine if the relationship is linear (r^2 near 1.00) and if the current form of the standard is appropriate for representing the continuum of health effects associated with increasing ozone concentrations.

Georgia Environmental Protection Division examined the current form of the standard against various integrated forms of the standard (average of the top 4 and average of the top 10 daily maximum 8-hour ozone average concentrations) at all 23 ozone monitors in the state of Georgia for 2013-2018. Comparisons were made for 3-year design values (DVs) for 2015-2018 which includes DVs for the following 3-year periods: 2013-2015, 2014-2016, 2015-2017, and 2016-2018. The ozone design value r^2 for the current form of the standard vs. the average of the top 4 daily maximum 8-hour ozone average concentrations was 0.963 (Figure 1). The ozone design value r^2 for the current form of the standard vs. the average of the top 10 daily maximum 8-hour ozone average concentrations was 0.979 (Figure 2).

This indicates that the current form of the standard may be appropriate to represent the upper part of the ozone concentration distribution in Georgia. However, it is not known if this is true in other states or other regions of the county. A similar type of analysis should be performed for the entire country (either state-by-state or region-by-region) to determine if the current form of the ozone standard is appropriate nation-wide.

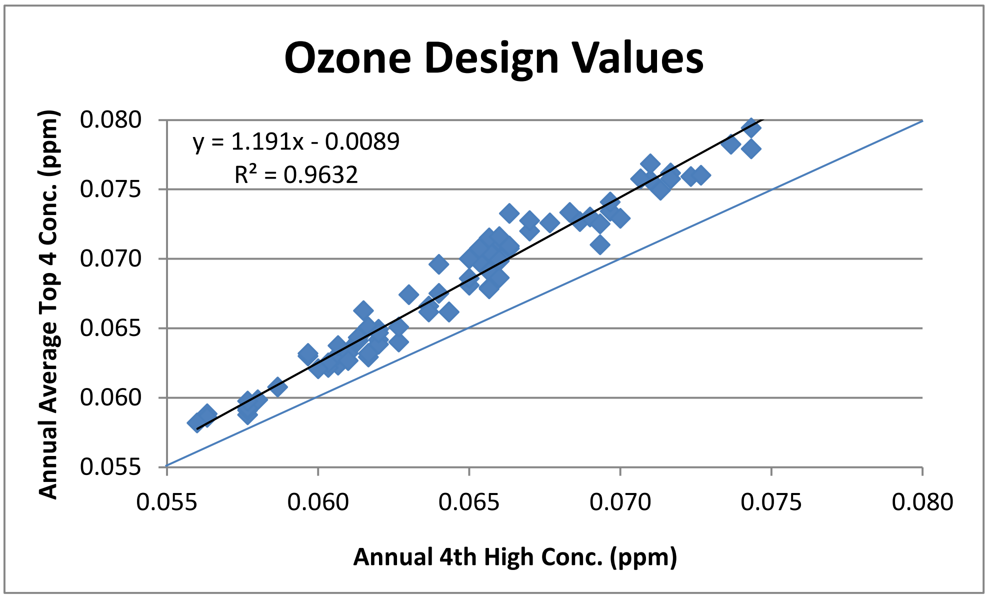


Figure 1. Comparison of the 3-year ozone design values (2015-2018) using the annual 4th high daily maximum 8-hour ozone average concentration vs. the annual average of the top 4 daily maximum 8-hour ozone average concentrations.

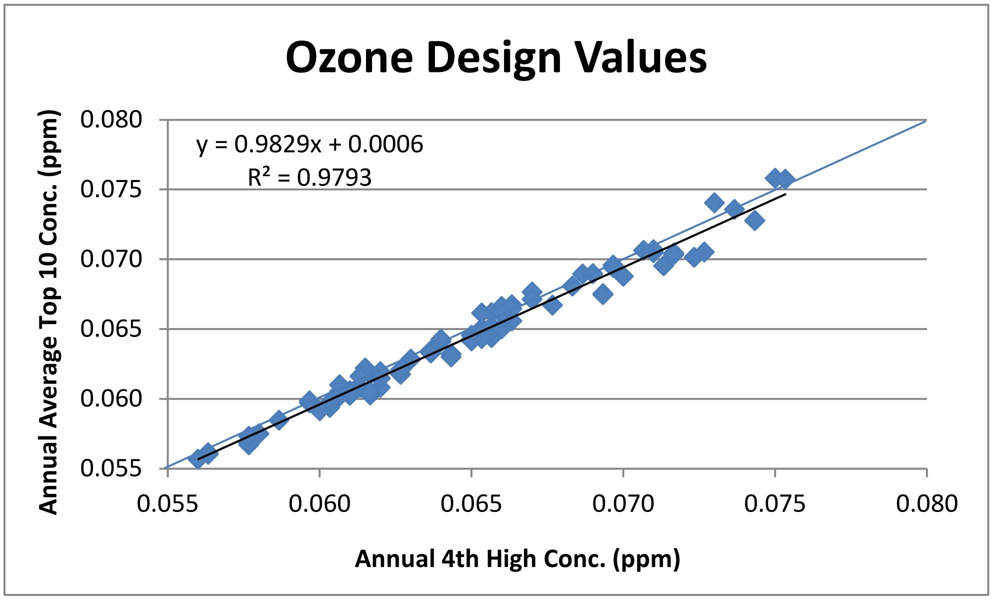


Figure 2. Comparison of the 3-year ozone design values (2015-2018) using the annual 4th high daily maximum 8-hour ozone average concentration vs. the annual average of the top 10 daily maximum 8-hour ozone average concentrations.

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary 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?

The approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary standard is sound and reasonable. The W126 index remains an appropriate metric for assessing cumulative ozone exposures with regard to potential concern or risk characterization. According to Table 4A-11, a median relative biomass loss (RBL) of 6.0% is associated with a W126 index between 23 and 24 ppm-hrs and a median RBL of 2.9% is associated with a W126 index of 17 ppm-hrs.

The PA states (page 4-102), "The evidence does not indicate single-year seasonal exposure in combination with the established E-R functions to be a better predictor of RBL than a seasonal exposure based on a multiyear average. Accordingly, it is reasonable to conclude that the evidence provides support for use of a multiyear average in assessing the level of protection provided by the current standard from cumulative seasonal exposures related to RBL of concern based on the established E-R functions." In addition, the use of a three-year average seasonal W126 index provides stability to the standard by recognizing that there is year-to-year variability in environmental factors (e.g., rainfall and meteorological factors) that influence the magnitude and distribution of ozone in any year.

2. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

Figure 4-12 contains a scatter plot of W126 (3-year average and annual values) versus 8-hour ozone design values based on 2018-2020 data. It shows that the seasonal W126 index values (3-year average) are at or below 17 ppm-hrs when the current standard is met at all 877 monitoring locations that were examined. Also, over 99% of single-year W126 values were at or below 19 ppm-hrs. The form and averaging time of the standard are not required to match those of the exposure metrics, as long as the standard, in all its elements, provides requisite protection against effects characterized for exposures of concern. Therefore, the current 8-hour ozone standard can be used as a surrogate for the W126 exposure metric.

In addition, any recommendation for an alternative secondary standard should be evaluated in the proper context of the standard to determine the adequacy of the alternative standard. In other words, all elements of the standard (indicator, averaging time, form, and level) and the way attainment with the standard is determined (i.e., highest design value in the CBSA) must be considered when determining the appropriate level for the standard. This is important because setting standards based on the highest design value in the CBSA results in a spatial concentration distribution across the CBSA that provides adequate protection at concentrations well below the level of the standard. Without this additional analysis, it is difficult to determine the adequacy of any alternative secondary standards.

Based on the information provided in the PA and the discussion provided in Section 4.5, I support the EPA staff preliminary conclusion that the body of evidence and the quantitative air quality and exposure analyses do not call into question the adequacy of the protection provided by the current secondary standard and the current secondary ozone standard should be retained without revision. The scientific body of evidence and the quantitative air quality and exposure analyses on which this reconsideration is based are largely unchanged since the 2015 and 2020 reviews. In the 2015 and 2020 reviews, the Administrator concluded that a secondary ozone standard of 70 ppb was requisite to protect the public welfare from any known or anticipated adverse effects. In addition, this conclusion is consistent with the recommendation from the 2020 CASAC where all seven CASAC members unanimously supported EPA's conclusion that the current secondary ozone standard should be retained without revision.

References

Fiore, AM; Oberman, JT; Lin, MY; Zhang, L; Clifton, OE; Jacob, DJ; Naik, V; Horowitz, LW; Pinto, JP; Milly, GP. (2014). Estimating North American background ozone in U.S. surface air with two independent global models: Variability, uncertainties, and recommendations. Atmos. Environ. 96: 284-300. http://dx.doi.org/10.1016/j.atmosenv.2014.07.045

Guo, JJ; Fiore, AM; Murray, LT; Jaffe, DA; Schnell, JL; Moore, CT; Milly, GP. (2018). Average versus high surface ozone levels over the continental USA: Model bias, background influences, and interannual variability. Atmos. Chem. Phys. 18: 12123-12140. http://dx.doi.org/10.5194/acp-18-12123-2018

Dr. Judith C. Chow

Chapter 2 – Air Quality

1. To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?

Chapter 2 provides a comprehensive review of O_3 chemistry, precursor emission sources, and ambient O_3 measurements, with most efforts made on U.S. background (USB) O_3. A few suggestions are provided in the following sections:

- Source Emissions

U.S. O_3 precursor emissions by sector in Figure 2-1 (page 2-6) based on the 2017 National Emissions Inventory (NEI) (U.S.EPA, 2021a) use source categories that differ from those of the 2014 NEI (Figure 2 C-1a, b, and c of Appendix C) presented in the 2020 O_3 ISA. U.S. Greenhouse Gas emissions are presented in four categories in Figure 2-1 (U.S.EPA, 2021b) as compared to six categories in Figure 2 C-1d. Table 1 shows source sector comparisons for O_3 precursors between those presented in the 2020 ISA and the 2023 PA. Although anthropogenic emissions show reductions, a common source sector naming convention needs to be established for cross comparison. Wildfires and agricultural prescribed fires accounted for 41% of total CO, and 16% of VOC emissions in 2017 NEI (Figure 2-1b), but this is not noted in Figure 2-2 (page 2-7) for US anthropogenic O_3 precursor emission trends, except for an increase in VOC from “other Anthropogenic sources”. The same source sectors should be used to examine long-term trends.

Table 1. Comparison of US O_3 Precursor Emissions by Sector between ISA and PA

(i)a NOx, VOCs, and CO by source-sector	
2017 NEI (U.S.EPA 2021a)	2014 NEI (U.S.EPA, 2018)
Highway Vehicles	On-Road Diesel Heavy Duty Vehicles and On-Road non-Diesel Light Duty Vehicles
Non-Road Mobile	Non-Road Equipment + Gasoline
Agriculture & Prescribed Fires	Prescribed Fires
Biogenics	Vegetation and Soil (Biogenics)
(ii) CH_4 by source sectors	
US Greenhouse Gas Emissions and Sinks (1990-2019)(U.S.EPA 2021b)	2016 US Inventory of Greenhouse (U.S.EPA, 2016)
Energy/Fossil Fuels	Sum of Natural Gas Systems, Petroleum Systems, and Coal Mining
Agriculture	Agriculture-Animal Husbandry
Waste Disposal/Landfills	Landfills
Others	Others

- Ambient Air Monitoring

Since EPA is participating in an international effort to improve O_3 measurements (i.e., from the current chemiluminescence by nitric oxide to the UV absorption cross-section (Galbally et al., 2013)) in 2024, EPA is encouraged to consider revising O_3 monitoring requirements. Figure 2-6 (page 2-12) shows only 11 states in the US conducting twelve months of monitoring, with eight months monitoring (March to October) in 27 states and six months monitoring (April to September) for Idaho and Montana. Pacific Northwest states (OR and WA), which are sometimes impacted by wildfires during spring and fall, are only required to measure O_3 from May to September. With unprecedented climate fluctuations in recent years, continuous monitoring year-round would provide valuable information on seasonal and annual trends and associated photooxidant exposures to humans and ecosystems. Both Figure 2-11 (page 2-19) and Figure 2-17 (page 2-27) show decreasing national trends in "Annual 4th highest MDA8" and "Annual 2nd highest MDA1" O_3 concentrations. With complete data from 2000 to 2020, Figure 2-11 includes 822 sites, whereas 834 sites are included in Figure 2-17. The same data sets and identical vertical scales are desired for cross comparison.

- U.S. Background (USB) O_3

Section 2.5 presents a good summary of USB O_3 sources and approaches to quantify USB O_3 for 2016 using the Community Multiscale Air Quality (CMAQ) model applied at hemispheric and regional scales. In addition to temporal and spatial characterization of O_3 contributions, Section 2.5.3 examines the combined seasonal and geographic impacts, along with border transport and topographic dependencies.

Section 2B.1.2.2 of Appendix 2B documents the Anthropogenic Emission Inventory. The international emissions inventory is synthesized from the Hemispheric Transport of Air Pollution Version 2 (EDGAR-HTAP v2) inventory. EDGAR-HTAP v2 and v4 were compared to the Tsinghua University inventory (Zhao et al., 2018) for Chinese emissions. However, inventories for India, global shipping, and global fire contributions were not discussed. As Figures 2B-29 and 2B-30 (pages 2B-42 and 2B-43) show international contributions of over 5-8 ppb O_3 in 2016 originating from India, China, shipping, as well as US/Canadian and US/Mexico cross-border transport, model input data and uncertainties associated with model estimates should be discussed.

Tables 2-3 to 2-6 (pages 2-62 to 2-64) summarize the predicted USB O_3 by regions and elevation. Summertime USB O_3 ranged from 20 ppb in the southeast to 38 ppb in the west and 39 ppb in the southwest based on NOAA's US climate regions (Figure 2B-1, page 2B-9). The Atmospheric Model Evaluation Tool (AMET, U.S.EPA, 2023) was used to calculate model performance statistics for MDA8 O_3 . Evaluations include comparisons to satellite retrievals, O_3 soundings, CASTNET, and AQS observations without considering observations from additional rural background sites. Section 2.5.2.2 acknowledged the comparison with the Tropospheric Ozone Assessment Report (TOAR) with Phase I database through 2014 without further discussion.

NOAA's Earth Systems Research Laboratories have been measuring O_3 at several global locations (e.g., Barrow, Alaska and Mauna Loa, Hawaii since 1973) that include 10 countries with 12 sites in the US (NOAA, 2023). Several recent publications showing increasing surface and tropospheric O_3 in Antarctica (Kumar et al., 2021), US remote locations (Cooper et al., 2020), and Europe (Tarasick et al., 2019) that are relevant to global climate changes. An example time series is shown in Figure 1. USB O_3 varied from ~10 ppb in American Samoa to ~45 ppb in Mauna Loa Trend analysis for the Mauna Loa site in Cooper et al (2020) reported a trend value of 1.3 ± 2.1 ppbv per decade, corresponding to a 6% (2.3 ppbv) increase since 2000. Observations for global remote sites, along with the long-term trend analysis (Parrish and Ennis, 2019; Parrish et al., 2020; Parrish et al., 2022) can be compared to the CMAQ model estimates (that is limited to 2016) to provide a better perspective on USB O_3. The effect of USB O_3 estimates for different U.S. regions and their impacts on the primary and secondary standards need to be clarified.

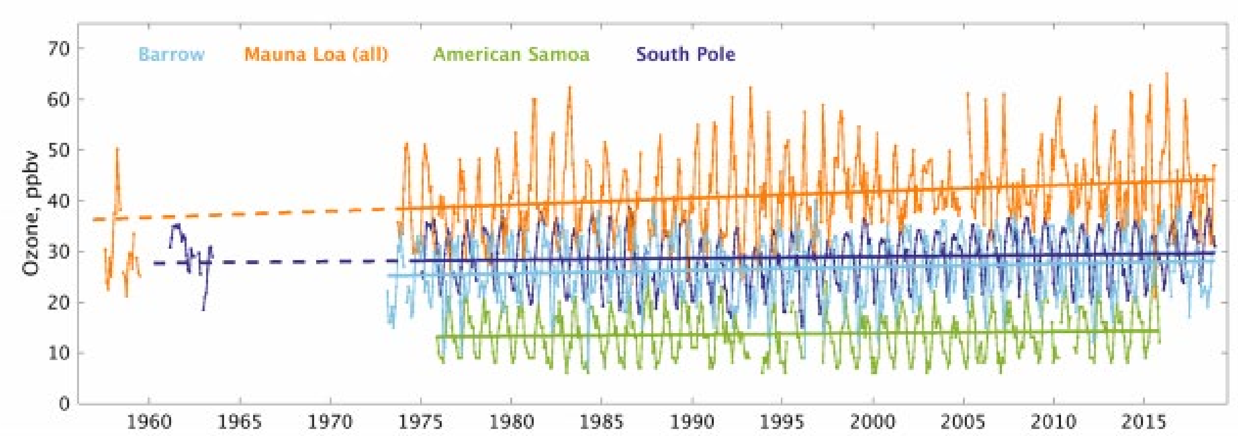


Figure 1. Time-series of monthly mean ozone at the four NOAA global monitoring laboratories (Cooper et al., 2020)

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Chapter 4 - Review of Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusion on the secondary 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?

- W126 Index Value and Relative Biomass Loss (RBL)

Chapter 4 provides an updated exposure/risk analysis to inform conclusions on the secondary standard. The exposure-response (E-R) relationships rely on the W126 index and relative biomass loss (RBL) as welfare indicators. Past results showing the sensitivity/susceptibility of plant responses to surface O_3 induced stress varied by environmental conditions and biochemical processes. However, there is a lack of standardized terminology and experimental protocols (Agathokleous and Saitanis, 2020). Impacts of O_3 on terrestrial ecosystems can also be estimated by process-based models that consider effects of O_3 fluxes on photosynthesis and plant tolerance (Tai et al., 2021). A combination of modeling (Ainsworth, 2017) with a concentration based metric (Mills et al., 2007) and/or flux based metrics (Mills et al., 2018a; Mills et al., 2018b) provide a weight-of-evidence that better represent O_3-induced impacts on ecosystems.

Establishment of E-R findings in Chapter 4 are limited to the 17 tree species derived from Lee et al. (2022) and Lee and Hogsett (1996), their representation of O_3 exposure to entire ecosystem and welfare effects need to be justified. Cumulative O_3 exposures (e.g., W126) and peak concentration occurrences (e.g., N100 metrics) are considered in the evaluation of growth-related effects and visible foliar injury. The choice of W126 index greater than 17 ppm-hrs only accounts for 7% (or 77 sites) of U.S. monitoring sites (2018-2020) that exceeded the threshold (Table 4D-3, page 4D-8 of Appendix D), much lower than the 34% (379 sites) at 7 ppm-hrs. When the W126 index is greater than 7 ppm-hrs, Table 4D-6 (page 4D-9) shows that 199 sites exceeded both the 4th maximum O_3 concentrations and the W126 value. Figure 4D-3 (page 4D-11) shows non-linear relationships between W126 and 4th maximum O_3 concentrations, the 17 ppm-hrs would not adequately protect the ecosystem for the southwest and western U.S. The association of the W126 index with a 6% RBL (median) to protect sensitive ecosystem needs to be clarified.

- Agriculture

Chapter 4 (page 4-22) indicates that evidence for agricultural crops is sufficient to infer a causal relationship between O_3 exposure and reduced crop yield and quality by citing IS.5.1.2, but IS 5.1.2 entitled "Whole-Plant Effects" (page IS-70 of U.S.EPA, 2020) does not address agricultural production. In addition, Section 5 of the ISA 2020 on "Evaluation of Welfare Effects of Ozone" lacks discussion on agricultural crops. Figure 4-3 (page 4-38) and Section 4.A.1.2 of Appendix 4A show relative yield loss (YRL) as a function of W126 (ppm-hrs) for the 10 crop species from Lee and Hogsett (1996) without much discussion. The Lee and Hogsett (1996) was not peer-reviewed.

Crop yield losses due to O_3 and implication for U.S. and global agriculture need discussion. Ainsworth (2017) estimated 2.6-17.7% and 3.9-15.6% of annual relative crop yield losses for North America and the World, respectively. Mills et al (2018b) estimated that O_3 reduced global yields by 4.4-12.4% for soybean, wheat, maize, and rice; totaling 227 Tg of loss per year. Using different exposure indicators (e.g., AOT40, SUM06, and W126), Figure 1 (Tai et al., 2021) shows lower estimate with W126 metric values. The estimated annual crop yield loss of soybean (~4-19%) and wheat (~2-15%) in U.S. (Tai et al., 2021) reveals the potential effects of O_3 pollution on agricultural production. Using the growing season average 7-hr O_3 (M7), Figure 2 shows great reduction in relative yield with increasing O_3 (Mills et al., 2018b). The adequacy of 70 ppb MDA8 O_3 to protect crop production and food security and its implications for public welfare warrants additional discussion.

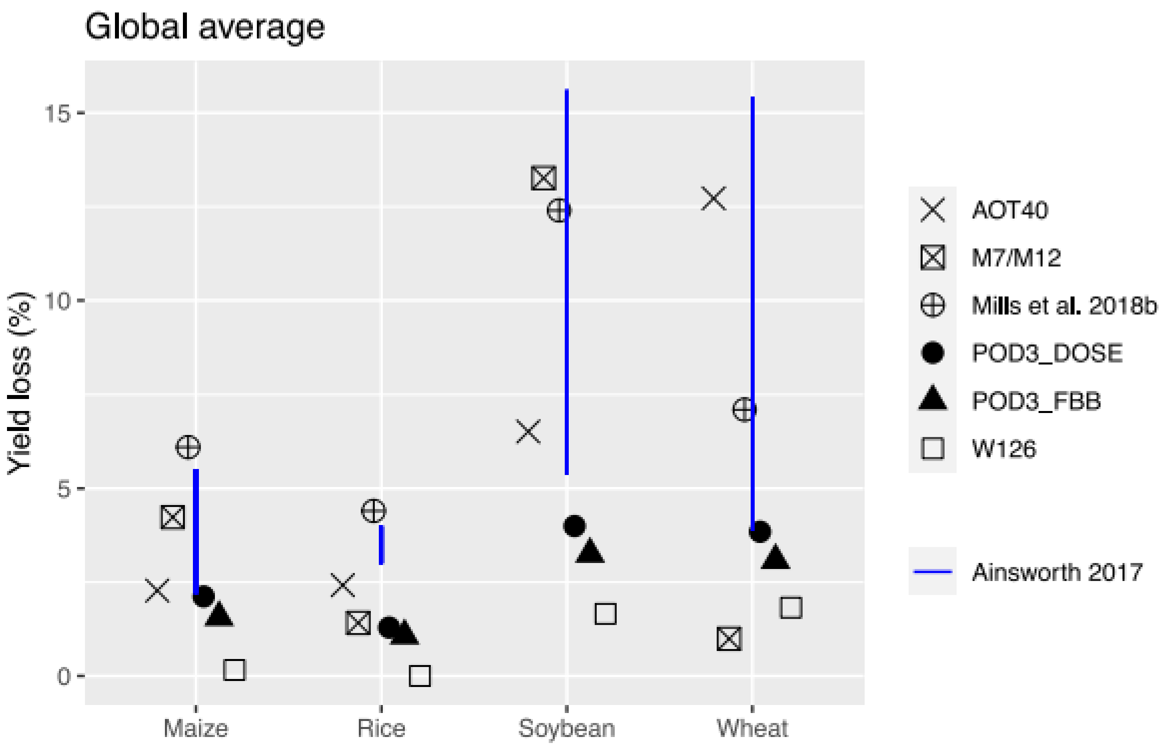

Figure 1. Aggregated global yield loss (%) estimates (Tai et al., 2021) for four major crops using different concentration based metrics (AOT40, M7/M12, W126, from Ainsworth et al., 2017) and flux based matrix (POD_3 and from Mills et al., 2018b).

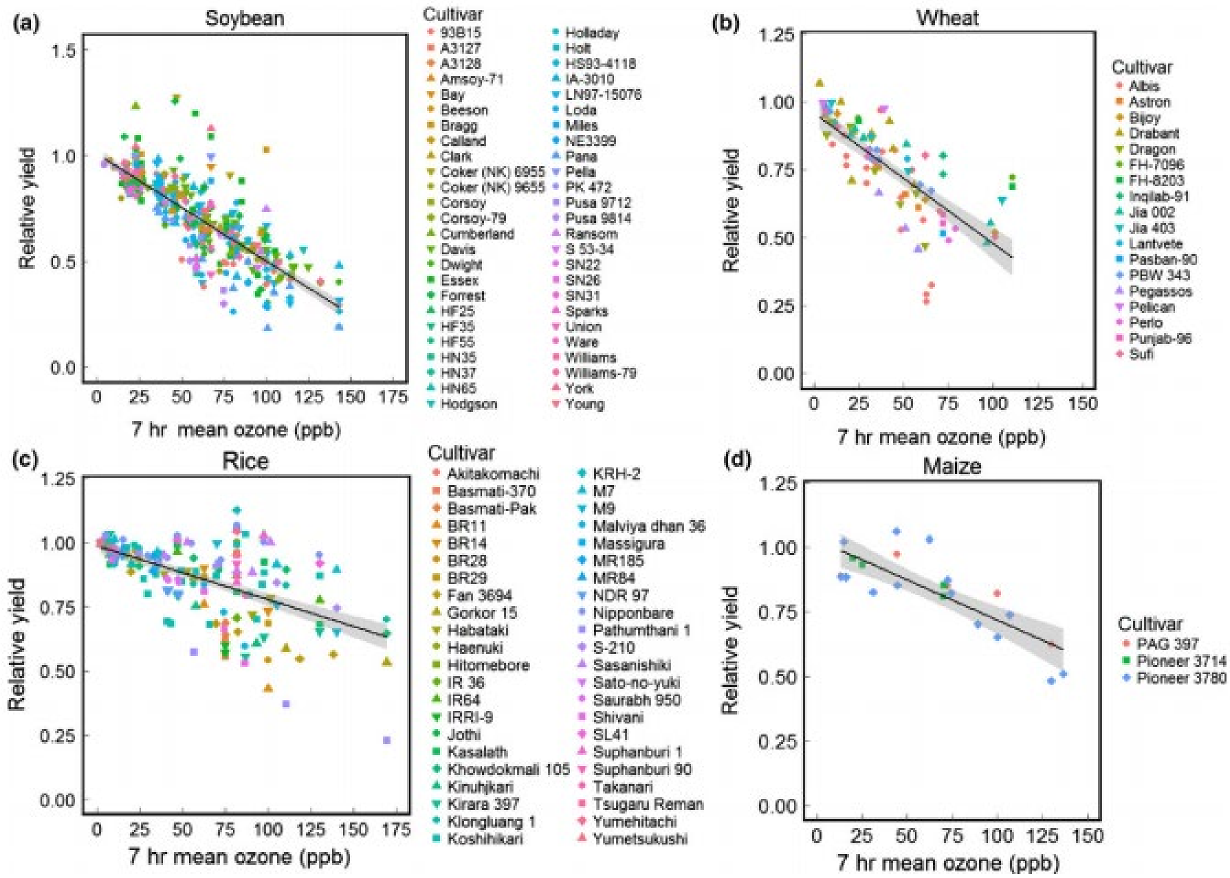

Figure 2. Response functions of relative yield as a function of 7 hr mean ozone for: a) soybean; b) wheat; c) rice; and d) maize (Mills et al., 2018b).

- Effects of Climate Change

Chapter 4 acknowledges the uncertainties in quantifying climate response to O_3 changes without elaborating on potential impacts of climate change on forest ecosystems and public welfare (e.g., Feng et al., 2021; Sonwani et al., 2022). Several studies point to a dependence between temperature and O_3, especially in the northeast and southeast regions of the U.S. (e.g., (Phalitnonkiat et al., 2018). Porter and Heald (2019) show temperature dependence of biogenic emissions contributed to 3% of the O_3-temperature correlations in the U.S. on average, with 6% and 10% on deposition and soil NO_x emissions. Higher O_3 concentrations during drought (Lee et al., 2023); climate change induced O_3-temperature penalty (Fu and Tian, 2019; Porter and Heald, 2019); and temperature-enhanced O_3 precursors (e.g., (Dewan and Lakhani, 2022; Nolte et al., 2021; Pommier et al., 2018) need to be considered as climate risk estimation with respect to the current O_3 standard.

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Dr. Mark Frampton

Chapter 3 – Review of the Primary Standard

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?

The approach taken in Chapter 3 of the current draft PA, summarized in Fig 3-1, is consistent with that taken in the draft 2020 PA, and in the 2015 review. The new draft responds to CASAC's comments on the 2020 ISA, in part by expanding the justification for this approach. The risk estimates have been revised, updated, and improved, and the presentation is clear. The estimates are not substantially different from the draft 2020 PA.

The risk assessment continues to be driven primarily by findings from the ozone controlled human exposure (CHE) studies, especially those conducted at concentrations most relevant to the current standard, i.e. those at 80, 70, and 60 ppb, for 6.6 hr with prolonged exercise. The summary in Chapter 3 of the ozone respiratory effects that are demonstrated in the CHE studies, based on those available in the 2020 review, is accurate. These have shown effects on airway function and inflammation at concentrations as low as 60 ppb in healthy young adults (Kim, Alexis et al. 2011). The PA acknowledges the limitations and uncertainties of this approach (Section 3.3.4), but justifies continued reliance on CHE data because they are the "most certain" (page 3-7). The strong epidemiological evidence for short-term respiratory health effects is excluded from the risk analysis on the basis that the majority of studies were conducted in areas that would not have met the current standard.

The risk analysis therefore is little changed from the 2020 draft, and not surprisingly comes to similar conclusions. The calculations based on careful and clearly detailed estimations of ozone exposure and time activity levels conclude that very few children with asthma would be exposed more than once per year to 70 ppb for 7 hours at moderate to heavy exercise, under conditions that meet the current standards. The PA concludes (P. 3-115) that "…available evidence and exposure/risk information do not call into question the adequacy of protection provided by the existing standard or the scientific and public health judgments that informed the 2020 decision to retain the current standard…".

However, there are reasonable alternatives to the risk assessment approach taken in the draft PA, that would provide substantially different estimates of the number of people at risk.

Following are three assumptions inherent in the PA risk assessment, and why those assumptions should be challenged.

Assumption #1. The epidemiological findings of increased ED visits and hospitalizations in children with asthma associated with increases in ozone exposure are driven by "high-end" exposure concentrations that would rarely be experienced in areas that meet the current standard.

This assumption is inherent in the argument in the draft PA to exclude the epidemiological studies from the risk assessment. The reasoning is stated on page 3-47, commenting on studies that do not meet the current standard: “In such instances, it is possible that the health outcomes associated with O_3 in the study are influenced wholly or in large part by concentrations above the level of the current standard.”

This is unlikely. The evidence from studies examining exposure-response relationships indicates that the effects observed in the epi studies are not driven “…wholly or in large part by concentrations above the level of the current standard.” Epidemiological studies that have examined ozone exposure-response relationships provide evidence that exposures below 60 ppm are associated with health effects. An example is the exposure-response curve in Figure 3-8 from the 2020 ISA, copied below. ED visits in Atlanta for children with asthma were studied in relation to ozone exposures (Strickland, Darrow et al. 2010). As described on page 3-76 of the ISA, “Visual inspections of the plots revealed approximately linear associations and no evidence of a threshold with 8-hour daily max ozone concentrations as low as 30 ppb…” The bulk of the data, with the narrowest confidence intervals, are in the range of 45 to 65 ppb. Other studies have shown similar concentration-response relationships, such as Zu et al. regarding hospital admissions in children and younger adults (Zu, Liu et al. 2017). These data contradict the contention that the findings in the studies conducted in areas that would not have met the standard were somehow driven by the highest concentrations.

The epidemiological evidence for short-term respiratory effects, taking into consideration the consistency of the findings across different locations and study designs, and considering the exposure-response data, argues strongly that adverse health effects are occurring in people with asthma, at concentrations that would be seen frequently under compliance with the current standard. Thus, excluding the epidemiological data represents an overly conservative approach that leads to underestimation of the number of individuals at risk.

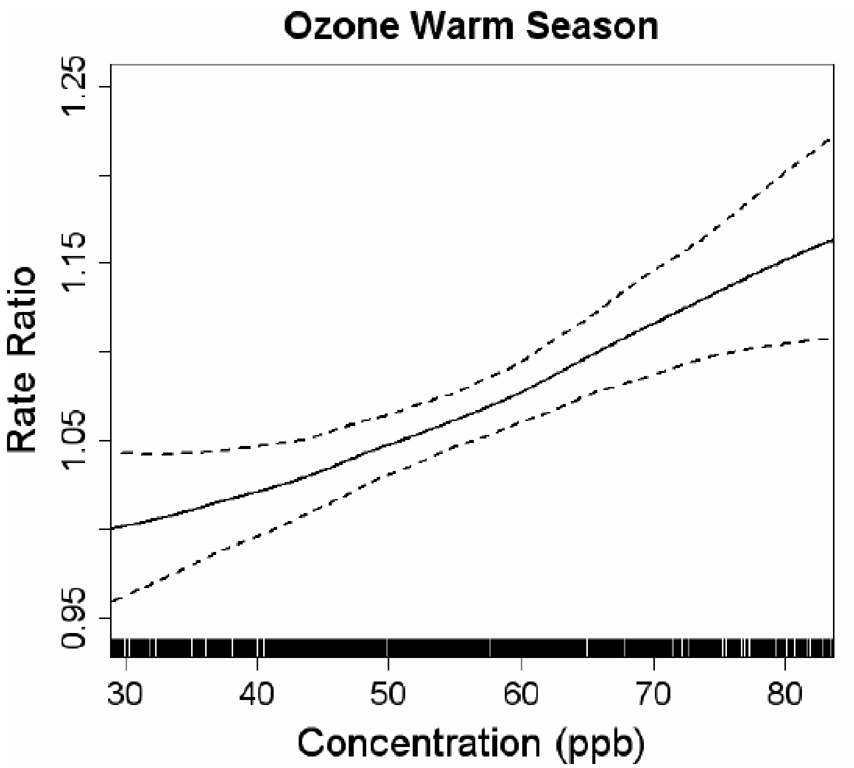

Figure 3-8 from the 2020 ozone ISA. Locally estimated scatterplot smoothing (LOESS) C-R estimates and twice-standard-error estimates from generalized additive models for associations between 8-hour max 3-day avg ozone concentrations and emergency department (ED) visits for pediatric asthma. Strickland et al. 2010.

Assumption #2. Moderate to heavy exercise is necessary during ozone exposures, at concentrations relevant to the standard, in order to experience adverse effects.

This is a long-held assumption that is based on the numerous CHE studies examining ozone lung function effects in healthy adults. The PA uses two different modeling approaches based on the CHE data to estimate lung function decrements with exposures to various concentrations, durations, and exercise levels. These models would not predict significant lung function decrements with exposures, at rest, to concentrations relevant to the current standard, in healthy people. As stated on page 3-40 of the draft PA: "For example, in studies of generally healthy young adults exposed while at rest for 2 hours, 500 ppb is the lowest concentration eliciting a statistically significant O_3-induced group mean lung function decrement". The assumption has been, therefore, that moderate to heavy exercise for multiple hours is necessary during exposure to ozone, at concentrations relevant to the standard, in order to cause decrements in lung function. However, as of 2020, there were no studies with participants exposed to ozone for 6.6 hours *at rest*, to confirm this assumed absence of effects.

Such a study has now been published (Hernandez, Ivins et al. 2021). 14 healthy young adults underwent resting exposures to 70 ppb ozone, or clean air, for 6.6 hours. FEV_1 decreased 2.8% relative to clean air control exposures, with evidence for increased airway inflammation. From Figure 2, panel B of that paper, shown below, it appears that 3 of 14 subjects had differential decreases in FEV_1 of about 10%. The study calls into question the assumption that moderate to heavy exercise is necessary for adverse health effects. It has important implications for the risk assessment. Even if EPA continues to exclude the epidemiology findings and restrict the basis for the risk assessment to the findings from the CHE studies, the estimates of the number of people with asthma with exposures of concern will need to be expanded to include resting exposures. The APEX exposure modeling will need to be modified to include all 7-hour benchmark exposures, regardless of exertion level. This indicates the current standard likely does not provide an adequate margin of safety for people with asthma and other respiratory diseases.

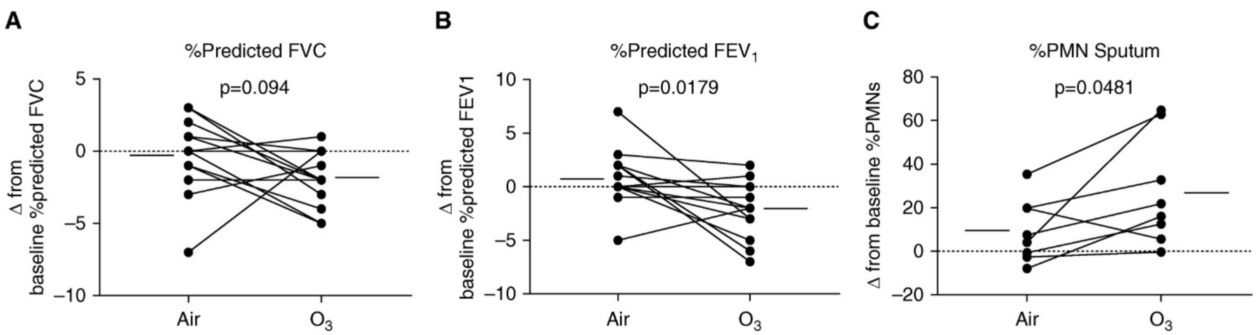

Figure 2. (A and B) Change from preexposure %predicted FVC (A) and FEV_1 (B) after 6.6-hour exposure to clean air (CA) or an average O_3 concentration of 70 ppb (n = 14). (C) Change from preexposure sputum PMNs of the O_3 and CA exposures (n = 8 paired sputum samples of sufficient quality for analyses). Horizontal bars in A–C denote the mean. O_3 = ozone; PMN = neutrophils (Hernandez, Ivins et al. 2021).

Assumption #3. The findings in the 6.6-hour CHE studies of healthy, young, physically-fit adults, showing no effects on symptoms at concentrations below 70 ppb and no lung function effects below 60 ppb, are relevant for and applicable to children with asthma.

Section 3.3.2, *Public Health Implications and At-risk Populations*, provides a good discussion of the potential health significance of ozone exposures in children with asthma, that is based on the ATS/ERS publications on the adversity of air pollution health effects (American Thoracic Society 2000, Thurston, Kipen et al. 2017). This section appropriately points out that small changes in lung function or increases in airway inflammation, as demonstrated in the CHE studies, may not be of concern for healthy individuals, but may be a significant risk for people with underlying lung disease, such as asthma. Even small increases in airway inflammation could presumably trigger an asthma exacerbation, because the disease is characterized by airway inflammation. The same is true for increases in airways responsiveness.

It remains unclear whether people with asthma, or other underlying airways diseases, experience greater changes in lung function in response to ozone, compared with people without airways disease. As pointed out in the PA, CHE studies of people with generally mild stable asthma have shown similar decrements in lung function as people without asthma. However, the studies of hikers on Mount Washington in the 1990s (Korrick, Neas et al. 1998) are relevant here. Day hikers on Mount Washington underwent spirometry before and after their hike. Decrements in lung function correlated with hourly ozone concentrations, and the relationship was robust to adjustment for $PM_{2.5}$ and aerosol acidity. Of note, hikers with a history of asthma or wheeze showed a fourfold greater decrease in FEV_1 than hikers without such a history. The highest quartile of exposure concentration had a mean of 50 ppb. These findings were included in the 2013 ISA, but not in the 2020 PA or this revised PA. The findings suggest that people with airways disease may experience substantially greater ozone-related effects with ambient exposures, compared with the CHE setting, and that effects are occurring below the current standard.

The PA acknowledges that children with asthma are at increased risk for adverse consequences from ozone exposure, with strong supporting evidence from studies of ED visits and hospital admissions for asthma, and correctly cites evidence that the developing respiratory tract may be especially at risk for airway remodeling effects and limitation of lung growth.

The PA concludes on page 3-30 that,

> "…consideration of differences in magnitude or severity, and also the relative transience or persistence of the responses (e.g., FEV_1 changes) and respiratory symptoms, as well as pre-existing sensitivity to effects on the respiratory system, and other factors, are important to characterizing implications for public health effects of an air pollutant such as O_3...".

Despite this thorough and important discussion, this issue is subsequently relatively ignored, and is not carried forward sufficiently to be incorporated into the risk assessment.

Conclusions for Charge Question 1

As stated in the PA, p. 3-113, "…different judgments might give greater weight to more uncertain aspects of the evidence or reflect a differing view with regard to margin of safety." But the PA underestimates the uncertainties of the CHE studies in defining absence of health effects at lower exposure levels and concentrations, i.e. at and below 70 ppb, in children and people with underlying lung disease, especially given the virtual absence of CHE data in children. As summarized above and in the 2020 ISA, there is quite convincing evidence from the epi studies that children with asthma are being adversely affected at concentrations at and below the current standard. The over-reliance on CHE data to establish a no-effect threshold, and to estimate numbers of people with exposures of concern, combined with complete exclusion of the epidemiological findings in the risk analysis, leads to underestimation of the public health risk associated with exposures under the current ozone standard. The risk assessment presented in the draft PA should be considered a most conservative approach. It is recommended that, in future reviews, this be accompanied by an alternative set of risk analyses that incorporates the findings of the epi studies, and the findings of Hernandez, et al., indicating that there are adverse respiratory effects of multi-hour exposures to 70 ppb at rest. This alternative analysis will likely give a very different estimate of the number of children and adults with asthma impacted at the benchmark exposure concentrations. The Administrator's considerations regarding the ozone standard will be best served by considering a fuller range of plausible possibilities, based on all relevant data.

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

There is a simpler way of thinking about whether the current standard is adequately protective, with an adequate margin of safety. We have human exposure studies that demonstrate reductions in pulmonary function and increases in airway inflammation at concentrations as low as 60 ppb, 10 ppb below the current ozone NAAQS. And the more recent human exposure study, Hernandez et al. 2021, importantly demonstrates decrements in lung function and increases in airway inflammation at 70 ppb for 6.6 hours, *at rest*. It is reasonable to conclude that even small changes in lung function and increases in airway inflammation could be adverse for people with asthma, as acknowledged in the PA. So, for the casual observer, it seems obvious that a standard of 70 ppb as an 8-hour average does not provide an adequate margin of safety for people with asthma, or for people with other underlying respiratory diseases.

The evidence available is already sufficient to conclude that the current standard is not protective with an adequate margin of safety. What constitutes an adequate margin of safety is not specified in the Clean Area Act. Given that there are statistically significant respiratory effects of ozone at 60 ppb with exercise, it would seem logical and necessary to reduce the 8-hour standard to at least that level.

Based on the scientific evidence currently available, it is concluded that the level of the current standard is not protective with an adequate margin of safety. Revising the level of the standard within a range of 55 to 60 ppb is more likely to be protective and to provide an adequate margin of safety. It is reasonable to retain the indicator, form, and averaging time of the current standard.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

Future research:

- Additional human exposure studies are needed at concentrations of 50-70 ppb, for multiple hours at rest, in healthy people, to confirm and expand the findings of Hernandez et al., in people with underlying respiratory disease, especially asthma, and in healthy children.
- Additional epidemiological studies are needed assessing short- and long-term effects under conditions that would meet the current standard.
- Consider CHE and panel studies using impulse oscillometry as a lung function outcome measure. This method can be easily be done even by young children, and may be a more sensitive indicator of small airways function, the airway region most affected by ozone.

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Dr. Christina H. Fuller

Chapter 3 – Review of the Primary Standard

Overarching Comments

I value the time and effort that EPA staff have put into developing this Policy Assessment (PA) for the Ozone Reconsideration. The document provides a detailed policy relevant analysis of the wealth of material from epidemiologic, controlled human exposure (CHE), and toxicological studies provided in the Integrated Science Assessment (ISA) and two subsequent staff reviews of studies published after the 2020 ISA assessment period (Luben et al 2020, Duffney et al 2022). Multiple endpoints from these studies were explored in the ISA, and the PA restricts its risk estimations to only a few respiratory effects deemed causal in the ISA. A large amount of data was collected and analyzed for the ISA and a smaller proportion was utilized in the PA. My responses to the charge questions are given below.

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?

(1) In my opinion controlled human exposure studies are weighed too heavily in the estimation of risks. CHEs are an excellent method to examine exposure-response as well as mechanisms of effect, however the exposure itself is not representative of ambient exposures that include other photochemical oxidants. Since the NAAQS standard is for ozone and other photochemical oxidants this merits inclusion of epidemiologic studies that are not restricted to ozone alone. There is no scientific evidence that CHEs are inherently more informative than epidemiologic data, although the explanation of and reliance on CHEs in the PA prioritizes their value. I find it to be too restrictive that the benchmark concentrations are driven only by CHE concentrations. The justification for the decision to exclude epidemiologic studies in the Policy Assessment is not sufficient. The EPA should incorporate both types of studies in risk estimation.

(2) Extrapolating CHE studies with adult participants to apply to children requires a strong justification and thorough explanation. Risk is estimated in the PA for children "if the simulated children had the same sensitivity as the controlled human exposure study subjects (page 3-79)". However, the risk for children if they did not have the same sensitivity as that of the CHE study subjects was not explored. Since, children are designated as an at-risk group it is highly likely that they are more sensitive. There is a large amount of evidence in the scientific literature that supports their more sensitive status. The absence of children from the reviewed CHE studies (and in the literature) is to me an "appreciable data limitation" and therefore, cannot be used in

risk estimation directly. Use of these studies would have to include some adjustment for the increased sensitivity of children, if it is possible to do so accurately.

(3) At-risk populations are described at length in the Ozone ISA and children (especially children with asthma) and outdoor workers were identified as those with the most evidence of increased risk. While risks of children are estimated in the PA (see previous), those of outdoor workers are omitted due to "appreciable data limitations." (Page 3-66). This explanation is insufficient and ignoring this at-risk group may result in an underestimate of the public's adverse impacts. Estimation of the risk for these populations, because some populations (e.g. asthmatic, outdoor workers) are at-risk due to a combination of innate/acquired susceptibility and vulnerability tied to exposures. The document includes a description of susceptibility and vulnerability as it pertains to at-risk populations in the footnote on page 3-18 of the PA.

(4) A better justification is needed in Section 3 for the selection of the eight cities included in the population exposure and risk modeling. Justification for selection of only these eight locations was neither compelling nor convincing. Restricting the analysis to urban areas precludes the estimation of risk in rural areas some of which could have higher ozone concentrations due to their downwind location from urban sources as well as high proportions of at-risk populations (e.g. outdoor workers).

(5) There are detailed maps on spatial concentrations (Appendix 3C), but a lack of incorporation of this information with populations, especially at-risk population including all asthmatic children and, in particular, black asthmatic children. These at-risk populations are not distributed equally in urban areas due to institutional and historical decisions like segregation and income. An acknowledgement of the uncertainties linked to the relationship between spatial variation in ozone and at-risk populations would bring value to the PA.

<u>Points of clarification or justification:</u>

Please state the focus of risk estimations on children, including those with asthma, up front. It was stated that it was the case for the 2015 and 2020 assessments (page 3-2), but not that it was so for the 2020 reconsideration.

I would suggest the inclusion of figures in addition to Tables 3-6 through 3-11.

Page 3-3, Lines 21-24. Suggest adding an additional sentence to clarify this point. To readers it may seem counterintuitive that higher exposure concentrations cause a lower response in people at rest and that lower concentrations cause greater effects at high ventilation.

Page 3-47. Describe what measurement data is used to calculate design values and is it representative of exposed populations. Assessment of design values based on all monitors versus one monitor.

Appendix 3C. It is difficult to distinguish between black circles and black dots in Figures 3C-2 to 3C-10. I suggest using another indicator to make the points more legible.

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

Please see comments for Charge Question 1. In addition, I have the comments below.

(1) Based on the analysis provided in the PA the level of 70 ppb is not sufficiently protective of public health. The protection should extend to at-risk groups (children with asthma and outdoor workers). Therefore, a level below the 70 ppb is necessary to provide protection of public health including at-risk groups.

(2) Design values being based on a single monitoring site eliminates information that could be utilized to evaluate adherence to the standard. An evaluation of the effect on risk models using one site compared to all applicable sites should be conducted and included in the PA. This sensitivity analysis would provide support for the use of a single site in the risk estimation compared to other approaches.

Additional text and clarification of the description of the data used to create Table 3-11 would be helpful in evaluating the results shown.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

There are detailed maps on spatial concentrations (Appendix 3C), but a lack of incorporation of this information with populations, especially at-risk populations (such as asthmatic children, black asthmatic children and outdoor workers). These at-risk populations may not be distributed equally in urban areas due to institutional and historical decisions that drive segregation and income inequities. Future reviews should estimate any added vulnerability to these populations due to spatial differentials in ozone concentrations.

Previous CASACs have identified the assessment of multi-pollutant exposures as an area to address. Current tools exist which have been designed to model multiple pollutant models as well as cumulative impacts. Exploring these news tools is advised for future policy assessments.

Dr. Terry Gordon

Chapter 3 – Review of the Primary Standard

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?

The presentation of the available data and the related uncertainties is done very well and clearly communicated, although minor edits to the Tables in the PA document and the Appendix are suggested (see Minor Comments below). In particular, the rationale and logic surrounding the uncertainties for the complete understanding and assessing of the effect of ozone on susceptible populations is, in general, clear and strong.

The presented rationale for relying on the controlled human exposure studies' data was strong, but the exclusion of consideration of the epidemiology data is concerning. While this ad hoc Panel member understands the uncertainties underlying the epidemiology studies, these studies have considerable strength and could be used more, in some way, to bolster the preliminary conclusion regarding the adequacy of the current standard. Moreover, the decision to not use the epidemiology evidence is puzzling given the strong statement on page 129, lines 8-14 which highlights that there are multiple studies with strong evidence linking ozone exposures with respiratory emergency department visits and hospital admissions. Similarly, the logic on lines 16-17 on page 142 could be turned around and it could be stated that epidemiology studies suggest a causal relationship between ozone and respiratory effects and that the controlled human exposure studies, using healthy individuals, support this conclusion.

The choice of the 8 cities used in the risk assessment is well justified but were additional information used in the decision to use the 8 cities? For example, why just eight cities? Were they the best available data? Was a sensitivity analysis performed to determine the optimal number of cities?

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

The logic behind the choice of ozone as the indicator for oxidant gases is strong and appropriate.

The rationale behind the choice of form seems appropriate but the underlying math is a bit beyond the expertise of this Committee member.

EPA's focus on adverse effects as signified by decrements in pulmonary function and respiratory symptoms is strong and logically justified. Along this line, the additional focus on multiple exposure scenarios being more important, from a public health perspective, is also well justified.

Given the epidemiology concentration response curve data showing hospital admissions for asthma, the exclusion of these studies seems inappropriate and should be utilized more fully in the risk analysis. If only used to support the controlled human exposure studies, they would point towards a lower than 70 ppb standard (which produced effects in healthy exercising adults) for active and outdoor asthmatic children. This suggests that a range of 55-65 ppb would be appropriate. Alternatively, if the epidemiology data itself was directly used to identify a protective level, the level could be different.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

The suggested additional research areas are very appropriate for reducing the identified uncertainties related to the ozone NAAQS. Top priorities, however, should go to: 1) more controlled human exposure studies of asthmatic individuals exposed at low levels of ozone (40 to 80 ppb); 2) children exposures – while controlled exposure studies in children are not likely to be done due to ethical reasons, more summer asthma camp studies would be useful; and 3) development of low cost ozone monitors for widespread use across the nation in order to reduce spatial exposure uncertainties.

Minor Comments:

a. Page 98, line 24 – Change determines to past tense?
b. Page 99, footnotes 2 and 4 – These are pretty important paragraphs and would fit well in the text rather than as footnotes.
c. Page 99, footnote 3 – Delete? Seems unnecessary.
d. Page 101, line 7 – It appears that a word is missing as this reads like a non-sentence.
e. Page 101, lines 14-15 – The use of the terms 'short-' and 'long'-term exposures is unclear. For example, does longer-term suggest greater than 8 hrs?
f. Page 103, lines 10-15 – A little redundant with the previous statement.
g. Page 104, line 24 – The text seems to jump between present and past tense on this page.
h. Page 115, Figure 3-1 – The text in the top 2 boxes are a bit out of focus. Also, the figure should be updated. While colorization isn't necessary, it is unclear what the shape of the boxes mean and they should be made more consistent/logical.
i. Page 118, lines 9-12 – The change in the causality statement for cardiac effects seems reasonable given the published studies, but have EPA staff considered Dr. Sheppard's rebuttal of the 'negative findings' studies that were used to reduce the cardiac causality statement? Also, the rationale for a causal relationship between ozone and metabolic changes is weak and the change is unwarranted. In particular, it is not logical to state elsewhere that the high animal ozone exposure levels don't lend strength to any exposure-response relationships for ozone and

respiratory effects and then use a few animal study publications at high concentrations to then justify a causal association for metabolism. Also, the bolstering of this causality determination by only 2 human studies is somewhat weak. This weakness (i.e., only 2 human studies) is actually stated by EPA in the PA (page 157, line 5).

j. Page 124, line 4 – ibid.
k. Page 127, lines 24-26 – Unclear sentence – It says expands and updates by retaining and then while retaining?
l. Page 130, lines 8-10 – Redundant with verbiage above.
m. Page 130, line 20 – It would be appropriate to mention the MOSES studies (controlled ozone exposure studies of older individuals) here.
n. Page 131, lines 4-5 – Incomplete sentence?
o. Page 131, line 29 – This seems a bit misleading. The focus on children brings together a wide range of age whereas the 20-24 yr old prevalence numbers are the highest for a 4 yr span.
p. Page 133, Table 3.1 – what is the black line under the number 88 for?
q. Page 134, line 7 – should this be ‘ethical or safety’ or ‘ethical and safety’?
r. Page 134, line 15 – add ‘personal’ before exposure.
s. Page 155, line 30 – insert ‘controlled human exposure’ before ‘studies’.
t. Page 163, line 20-21 – This sentence’s logic is unclear - wouldn’t an ozone monitor already be measuring ozone accurately regardless of NOx-related reduction of ozone? Is this double correcting?
u. Page 166, line 7 – The ref says (0).
v. Page 171, footnote 91 – It is unclear what is meant by ‘most recent’ – how does this identify an update since the 2015 Review yet reference a 2013 paper?
w. Page 176, line 12 – Please add something here to clarify how this works than stating the ‘just met’ scenario? Perhaps provide a rationale here as to how the 75 and 65 ppb design values add to the risk assessment.
x. Page 177, lines 30-32 – Unclear statement.
y. Page 184, Table 3-9 – Is this percent of child population or child asthmatic population?
z. Page 187, lines 12-13 – This appears unclear (or I am reading it backwards; ignore if so) – it seems to state that the estimates increase for 75 ppb for the 60 ppb benchmark compared to the 70 ppb benchmark.
aa. Page 191, lines 12-14 – Again, the rationale for the metabolism causality statement is very weak.
bb. Page 192, line 18 – This is unclear and not quite accurate - everything referenced in Section 3.3.3 is from 2012 and before.
cc. Page 194, line 22 – Add a reference to the appropriate table/figure in the Appendix.
dd. Page 197, Table 3-11 – The first column uses DV whereas Design Value is the term used in the legend.

Dr. Catherine Karr

Chapter 3 – Review of the Primary Standard

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

The PA does well in recognizing the robust evidence that identifies children and children with asthma among the most sensitive populations to ozone respiratory health effects. The PA also underscores the limitations of the human controlled exposure studies (HCE) to represent the populations not represented in such data, in particular children and children with asthma. The PA also recognizes the strong evidence for longer term ozone exposure in early life influencing lifelong permanent health compromise including reduced lung functional development and development of chronic disease for which we have no cure (i.e. asthma). Despite this, the PA conclusions are overly and narrowly focused on the controlled human exposure studies of short term respiratory effects to ascertain the health effects of ozone across the population and evaluate the current standard.

By design HCE data are inadequate to inform pediatric health effects. Furthermore, they are inadequate to inform the very concerning public health outcomes associated with early life exposure to ozone on reduction of attained adult lung function and development of asthma in childhood. These data are also inadequate in informing health impacts in individuals who are marginalized or experiencing poverty, with existing evidence suggesting higher ozone impacts in such populations.

A comprehensive "overall evidence view" in evaluating the standard requires meaningfully recognizing not just the HCE data but also the sizable epidemiologic evidence supporting enhanced toxicity and health concerns for infants and children, children with asthma, and marginalized, low resourced communities into decision-making. The HCE data demonstrates lung function effects at 60 ppb for healthy adults. Greater effects on lung function as well as effects on symptoms are demonstrated in those studies at the current standard of 70 ppb. A complementary line of evidence is noted in the Table summarizing ozone short term respiratory effects in the ISA (Table IS-4), which states "Evidence from many recent, large multicity epidemiologic studies provide further support for an association between ozone and ED visits and hospital admissions for asthma; associations are generally strongest in magnitude for children between the ages of 5 and 18 y ears in studies with mean 8-h daily max ozone concentrations between **31 and 54 ppb**. Additional epidemiologic evidence for associations between ozone and hospital admissions and ED visits for combinations of respiratory diseases (**31** to **50 ppb** as the study mean 8-h daily max). Integration of these lines of evidence does not support the conclusion that children, and children with asthma are protected under the current standard of 70 ppb.

The PA could be improved by representing the epidemiological evidence for respiratory effect in exposure and risk analyses. This robust evidence base should not be viewed as "limited" in its ability to inform the standard and protection, rather this is a "highly informative" evidence base given the consistency of the findings across different locations and study designs, considering the exposure-response data, and data that strongly argues adverse health effects are occurring in individuals with asthma, at concentrations that are below the current standard.

An overall evidence view would suggest it is most reasonable to infer that health effects observed among healthy adults exposed for short durations while active at 60 and 70 ppb will not be the same for populations identified as more sensitive and not captured by these HCE data. It is highly reasonable to anticipate that exposure to children or children with asthma in scenarios such as presented in the adult HCE studies would result in adverse health effects and more impactful health effects. Indeed, the epidemiological studies demonstrate this as summarized in the ISA Table IS-4. The greater mean impacts on children and marginalized groups should be incorporated in determining whether the current standard is protective for the broad population. An overall evidence view, including observed linear dose-response of ozone respiratory health outcomes in experimental and observational studies such as Strickland et al, 2010, support that a lower standard of will more adequately protective of the broader population, including children.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

I agree with the research needs identified in the PA. I would recommend a few additional emphasis areas to inform future consideration of the protectiveness of the standard. The unique vulnerability of the fetus (exposure during pregnancy) and child to developmental toxicity and long term health compromise from early life exposure to ozone should be an important research focus. Continued refinement to characterize the influence of ozone on lung function development as well as development of atopic disease/disorders or other chronic conditions would be helpful for ensuring adequate protection of human health across the life course. The vulnerability of preterm infants (~10% of births in the U.S.) and infants who experience bronchiolitis (~10-15% of U.S. infants, ~1-3% hospitalized) should be characterized, as these groups are at high risk of developing chronic respiratory conditions such as asthma.

Mixture or joint effects analyses are needed. It would be informative to understand exposure to other contaminants as potential risk factors that could moderate ozone exposure risk (adversely or offer protection), much like SES, life stage, or pre-existing disease have been demonstrated. This is an underpinning of environmental justice concerns for the many communities that bear the double or triple jeopardy of socioeconomic stressors and other structural inequities and greater exposures to multiple contaminants including ozone.

Dr. Michael T. Kleinman

Chapter 1 – Introduction

1. To what extent does the Panel find that the information in Chapter 1 is clearly presented and provides useful context for this reconsideration?

The chapter provides an historical perspective on the evolution of the O3 standard. It adequately lays out the points to be considered in setting the standard:

a. Requisite to protect public health and welfare.
b. May not consider the costs of implementation.
c. Does not consider attainability and technical feasibility.
d. Provides an adequate margin of safety intended to address uncertainties associated with inconclusive scientific and technical information available at the time of setting the standard.

A key statement is that in selecting "primary standards that include an adequate margin of safety, the Administrator is seeking not only to prevent pollution levels that have been demonstrated to be harmful but also to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree."

These considerations should be in the forefront of our review of the recommendations on the range of the primary and secondary standards.

Chapter 2 – Air Quality

1. To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?

The chapter provides a good summary of design values and their trends. There was some discussion of wildfires and the finding that current models may over predict WF O3 impacts, which may be more important in the western states. However, the impact of wildfires on short term peak O3 concentrations might be discussed more fully. Also, by EPA's own reckoning, climate change may be expected to increase the frequency and intensity of WFs; some discussion of the implications of this on potential exposures would be useful.

Chapter 3 – Review of the Primary Standard

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

The 2015 standard (which was retained in 2020) was driven by "respiratory effects from controlled human exposure studies…" In the 2020 ISA, cardiovascular effects and mortality were deemed to be too weak to support the 2015 conclusion of being likely to be causal and in the 2020 assessment the data supporting these endpoints were "suggestive, but not sufficient to infer a causal relationship." This conclusion was influenced by the downgrading of population and epidemiological studies, which is pervasive in the ISA and PA.

The retention of the 8-hr averaging time at 70 ppb was estimated to protect the vast majority of children (96% to 99%) from experiencing two or more days with exposures at or above 60 ppb with an adequate margin of safety.

It should also be noted that there is a disparity in asthma prevalence; people who are black non-Hispanic, and/or living in households below the poverty level, are 50 to 100% more likely to have asthma than others (PA 3-36 to 3-37). Therefore, the 1 to 4% of individuals in the "not protected" group may represent black or poor individuals, disproportionally.

The retention of the 70 ppb standard was largely based on extrapolations of data from short-term exposures of mostly healthy adults in controlled human exposures. The extent to which these extrapolations adjust for, and account for, the variance in human sensitivities within the population at large, is not well described. One concern is that children with asthma are at greater risk of O3-related effects and those effects are likely to be more severe than those effects experienced by adults, even those with mild asthma tested in the controlled human exposure (CHE) studies, i.e. children's responses may be quantitatively and qualitatively different from the adult responses. This may also apply to adults with more severe asthma who would not be candidates for CHE's. How the extrapolations of the data from CHEs take into account margin of safety considerations needs to be explained more explicitly. In fact, the evidence from CHE and epidemiological studies there is no evidence of a threshold for O3 effects down to 30 ppb (stated in the ISA). The cumulative evidence from the population and epidemiological studies support reconsidering the level of the standard and that the margin of safety afforded by the current standard is not adequate.

As per pages 3-31 to 3-32, the PA discounts the findings of epidemiology and population studies while emphasizing the controlled human exposure studies but the arguments for this should be reconsidered. The risk analysis was made without considering the epidemiological evidence from studies that demonstrated significant health effects even when the exposures were limited to those below the current standard.

For example the statement "[epidemiologic studies] utilize ambient air concentrations at monitoring sites as surrogates for exposure". This is a drawback but the purpose of the standard setting exercise is to determine the O3 concentrations at equivalent monitoring sites that will protect people from O3-related health effects. Using those sites as exposure metrics might be less of an uncertainty factor than using extrapolations of data from the limited population in controlled human studies.

Also, the point was raised that population studies involve "concurrent exposures to all pollutants in ambient air…" This is true, but several studies have reported using multipollutant model approaches in which O3 is determined to have an independent effect.

There is an inconsistency in the EPA approach to setting the PM2.5 standard compared to setting the O3 standard. In the former, the causality and standard range considerations were heavily influenced by population studies and used data from fixed site monitors as the exposure metric. For the O3 standard, population studies were discounted and controlled human exposures were deemed more important.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

The PA identifies several research needs, all of which should be considered. In addition, efforts should be increased to use the more granular data that could be obtained using large numbers of relatively inexpensive networked monitors that are now on the market. The quality of data obtained using these instruments has improved and assigning more resources to determine how to best exploit these instruments and their data is warranted.

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary 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?

Is the decision to reject the W126 index as the form and averaging time for the secondary standard (≤ 17 ppm-hr; 3 yr W126 average) warranted? The idea behind the W126 was that it better protected against cumulative O3 effects than did the 8 hr standard. The PA asserts that the primary 70 ppb standard would meet the W126 standard's level of protection under most situations, based on modeling. However, more analysis of the past several years of data and more discussion about those situations in which the W126 might provide protection that the 70 ppb standard would not protect against cumulative injury would help in our evaluation. Also, it would be helpful to add some discussion of the actual, or practical, benefit to reversing or discarding a standard that has been in place for close to a decade.

Some summary should be included in the PA of the discussion of why other aspects of possible welfare effects, such as O3's role in forming secondary organic aerosols that impact visibility or in the acidification of soil and lakes and water sources were not considered in the secondary standard.

Dr. Danica Lombardozzi

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary 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?

The EPA synthesized data from previous and new studies to understand:

- Relative biomass loss (RBL) and relative yield loss (RYL) in trees and crops using Lee and Hogsett (1996) and Lee et al. (2022)
- Visible foliar injury using data from the US Forest Service Biosites
- Comparison of the primary and secondary standards at EPA monitoring sites.

The data used in the synthesis uses the most recent available information for W126. The evaluation of available information, including key considerations as well as uncertainty and associated limitations, need to account for the following points:

- It is counter-intuitive that the median percent reduction for the combination of studies is lower in some W126 categories (17, 19, and 21 ppm-hrs) than for each individual study. Perhaps the median is not the best estimate of damage and a different metric, such as considering the quartiles, should be considered.

- The data for evaluating a three-year averaging period for the secondary standard only considered tree species. It did not evaluate other forms of vegetation that may not live for a full three years (for example, annual plants which are a large portion of vegetation in the Midwestern US) nor other metrics like RYL. Additionally, other related ecosystem consequences should be considered at a one- versus three-year time horizon. Ignoring these considerations could adversely impact public welfare.

- The EPA finds that the 3-year average W126 is at or below 17 ppm-hrs at all areas meeting the current standard. Does this change if a 1-year average is considered? Does it change if a lower W126 threshold, for example 9.2 ppm-hrs, is considered?

2. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

Section 4.5 provides rationale to support staff's preliminary conclusions. Potential alternative options should consider the following points:

- There is a need for a W126 secondary standard metric. While the existing standard may meet the W126 19ppm-hrs category, as illustrated by the updated analysis, the W126 threshold needs to be lower, ideally 9.2 ppm-hrs or less, to protect sensitive plants.

- There is a need for a 1-year averaging time period to protect annual plants and crops.

- There should be additional consideration for adding a peak concentration, such as N100, component to the secondary standard.

3. What are the Panel's views regarding the areas for additional research identified in section 4.6? Are there additional areas that should be highlighted?

The EPA highlighted several areas of additional research that are necessary to improve our understanding of plant protection. The points below, several of which overlap with areas identified in section 4.6, are recommended for priority consideration:

- RBL for additional types of vegetation. For example, there is little to no information included in the current analysis of RBL in grasses, so currently a large portion of the Great Plains is not represented in the current data.

- RBL for different age categories and species

- RYL in major agricultural crops, especially with regards to the effects of major management regimes such as fertilization and irrigation.

- The role of environmental drivers (temperature, precipitation, irradiance, etc.) on RBL, RYL, and visible foliar injury

- The role of peak ozone concentration on RBL, RYL, and visible foliar injury, as well as exposure studies that mimic realistic ozone conditions.

- Stomatal-based ozone metrics (e.g., cumulative uptake) and response relationships

- Community composition, species diversity, & biodiversity changes. This includes a variety of processes such as shifts in populations and genotypes, changes to soil nutrient and water availability, and other cascading ecosystem (e.g., changes in carbon and water cycling) and trophic (e.g., changes in herbivory presence and health) interactions.

- Impacts on pollinators and plant reproduction.

Dr. Howard Neufeld

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary 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?

The PA document details the history of the establishment of the current secondary standard and the reasons for the current level, averaging time, and form. There was discussion of the benefits of having a single season cumulative secondary standard, as has been recommended in the past by the CASAC, versus a 3-year cumulative index. The EPA describes the process by which the Administrator at the time noted that to keep the median RBL (relative biomass loss for trees) at 6% or lower required a W126 exposure index of 19 ppm-hrs (pg 227) but that if a 3-year average W126 index was to be used, it should be lowered to 17 ppm-hrs, as the CASAC recommended at that time. Doing so would virtually eliminate exposures that could result in 6% or greater RBL. EPA notes also that the Administrator determined that it would be appropriate to consider additional metrics, particularly the number of hours or days with $O_3 \geq 100$ ppb. As noted throughout the current PA, there can be instances where two different W126 indices of similar value differ substantially in the number of peak hours with $O_3 \geq 100$ ppb, and that it is these higher exposure levels that have been shown to be damaging to plants.

Later on, in the PA (pgs 231-232) EPA states that further analyses of the current 3-year 4th highest 8-hr average was "*more effective*" than the W126 index with regard to limiting the number of hours and days with peak concentrations, and that a single year standard was not sufficient to provide protection against such "*unusually damaging years*". EPA also states that the current standard would also provide adequate protection against RYL (relative yield loss) for agricultural crops. RBL values were initially based on exposure-response relationships for 11 tree species. Further discussion in this section of the PA extended the number of species to 16 based on the recently published paper by Lee et al. (2022). However, EPA bases its conclusions using the median of exposure responses, while Lee et al. (2022) conclude that sensitive species suffer RBL at W126 of 9 ppm-hrs or lower. Furthermore, crops and native annuals are responsive to ozone in the current year and a 3-yr average may not be protective of such vegetation.

Visible foliar injury, while extensively discussed throughout the PA, was not deemed sufficiently studied to be of use in determining the setting of standards, due to an inability to generalize across regions and species, and because many studies were not designed in a way that allowed a determination of the impact on public welfare. In addition, the links between visible foliar injury and alterations in growth and physiology were insufficient to allow determination of public welfare impacts. Thus, this parameter was not as useful as either the RBL for trees or the RYL for crops, where relationships between ozone exposure and public welfare were more determinative. I agree with EPA's conclusions regarding visible foliar injury.

EPA provided evidence for causal relationships for factors such as visible foliar injury, reduced tree growth, both reduced quantity and quality of crop yields, lowered plant reproduction, and alteration of terrestrial ecosystem functioning with exposure to O_3. For additional factors, such as tree mortality, alteration of ecosystem hydrology, and reduced carbon sequestration, relationships were determined likely to be causal, and EPA notes that establishing higher levels of association are technically difficult to achieve, even if they do occur. Therefore, these latter impacts are not at present adequate for setting the secondary standard. Insect-plant interactions were extensively discussed also, including alterations in feeding behavior and plant signaling, but currently there are too few studies of this subject and uncertainties are too high for them to be used to determine if the secondary standard should be changed.

The graphics used throughout this section of the PA are informative and generally well done. The way that the exposure-response functions were analyzed (e.g., Lee and Hogsett 1996, Lee et al. 2022) was well explained and it is clear to the reader how conclusions about the sensitivities of trees to O_3 exposure were evaluated. Uncertainties were also clearly stated (e.g., see page 276). Of particular concern is whether a single exposure-response function for any species can be extrapolated to multiple years of exposure. Only a few studies have followed trees for multiple years, and when done on trees grown in pots instead of rooted in the ground, additional factors come into play, because as the trees become larger, they can get root-bound, and that can influence responses in later years. For the few multiple year studies available, EPA concluded that a 1-year function was adequate to describe effects in subsequent years, but this is based on very few studies. However, Lee at al. (2022) also concluded that single year exposures were valid for establishing exposure-response relationships, and I agree with their and EPA's conclusions on this. In addition, there is uncertainty associated with extrapolating impacts on seedlings/saplings to large, mature trees, something that has been discussed many times in the past, but for which there are few technical solutions for exposing large trees to O_3, and few funding opportunities to conduct such studies because of the costs involved.

There was extensive discussion of the fact that agricultural practices could alter responses of crops to O_3, thus making it difficult to assess the relevance of some RYL functions. It is this section that is perhaps the least well explained, as the PA does not explicitly document exactly what agricultural practices they are referring to, nor the mechanisms by which they would alter crop responses to O_3. EPA should refer in more detail to the NCLAN (National Crop Loss Assessment Network) summaries, which are the most robust and thorough studies of ozone effects on crop yields. The most obvious actions might be application of additional fertilizers (there is some evidence of increased O_3 resistance with high levels of nitrogen), or farmers might change crop varieties which differ in O_3 tolerance/resistance. There is also a known reluctance by some farmers to switch to more O_3-tolerant crops (such as with soybeans) due to uncertainties regarding yields of these specialized strains.

EPA thoroughly analyzes the relationships between design values and annual and 3-year cumulative W126 exposures, showing that when the current secondary standard is lower, so is the W126. For meeting the current secondary standard, W126 values are nearly always below 13 ppm-hrs outside the West and Southwest regions. Furthermore, regions with the highest W126 also declined at faster rates as their design values declined, suggesting that in areas not meeting current standards, they would do so with further reductions as the design values fall (pg 292). Peak concentrations are kept at very low numbers also, ranging from 1 to 10 hrs for sites not meeting the current standard and are low at sites meeting the current standard. EPA states (pg 295) that the W126 metric has less potential to control these peak concentrations than the current secondary standard. This is only true, though, if the higher W126 of 17 ppm-hrs is used. With a lower value, most if not all concern about peak concentrations would be eliminated.

EPA also documents that among 877 sites with adequate O_3 data that meet the current standard, 99% of single-year W126 values differ from a 3-year average by no more than 5 ppm-hrs. All sites meeting the current standard also had W126 at or below 13 ppm-hrs, with very few reaching 19 ppm-hrs in earlier years. Later on, EPA states "*well over 99% of monitoring sites and periods when the standard is met….annual W126 values are less than 19 ppm-hrs*" (pg 302). Furthermore, using the median RBL derived from the 16 tree species analyzed in Lee et al. (2022) a 3-year W126 for sites meeting the current design standard would result in RBLs ranging from 2.9-5.3%, with few exceptions.

In summary, EPA states unequivocally that when all the evidence is considered, the current secondary standard meets the requirements of being requisite to protect the public welfare, and uses a similar argument for protecting against RBL for trees. As noted on page 353: "*In light of all these factors, we do not find the available information to call into question the adequacy of protection afforded by the current standard for crop yield-related effects*." However, EPA is basing this statement on a W126 of 17 ppm-hrs, which only protects half the species of trees evaluated (it is the median value). If a lower W126 is used, i.e., 9-10 ppm-hrs or less, then this statement would no longer be true.

Lastly, <u>EPA does admit that the W126 metric can be appropriate for assessing exposure responses of vegetation and for determining effects on public welfare,</u> but only when used in combination with peak O_3 concentrations, and importantly, EPA mentions that the secondary standard does not necessarily have to be the same as the primary standard (pg 354). I would agree with the previous statement, but only when a W126 of 17 ppm-hrs is being considered. As noted earlier, if a lower W126 value is used, 9-10 ppm-hrs, this virtually eliminates any problems caused by sporadic occurrences of high ozone concentrations and in this case, the secondary standard could utilize the W126 without having to consider them.

Typo:
Note on page 251, 5th line in next to last paragraph, "*The Agency*" is repeated twice in succession.

2. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

Some aspects of this question were answered in the response to question 1 above. To summarize, EPA does make a strong argument that the current secondary standard is requisite to protect the public welfare but leaves open the possibility of adopting a more physiologically relevant standard, such as the cumulative W126 exposure index, but only when coupled with another metric that documents the occurrence of peak O_3 concentrations. It does not specifically state what a peak concentration metric should be (e.g., how many hours, the timing of those concentrations, whether daily or seasonally, a rationale for what constitutes a "peak" concentration, whether they occur consecutively or not, or how to account for respite periods between peak occurrences. For this reason, I do not think a secondary standard can at this time incorporate a peak ozone requirement.

The other major consideration is whether the secondary standard should be for 1 year or averaged over 3 years. There is considerable discussion of the adequacy of the current secondary standard to protect vegetation against detrimental O_3 impacts, and which measured responses are causal or likely causal, as well as whether certain factors can be used to judge if the public welfare is protected in a requisite manner. For annual crops, a 3-year average could leave open the possibility of detrimental impacts in one year that are not accounted for when averaged over 3 years. However, the trade-off for a 1-year standard might be a lack of stability in assessing whether a region is in compliance or not versus the benefit of increased stability to protect against public welfare detriments. I would suggest that a 1-yr secondary standard could be created that is both more protective and stable (see below).

Based on Lee et al. (2022) and NCLAN results for RBL and RYL, respectively, EPA should adopt a new secondary standard, utilizing the W126 weighted index, cumulated over a 92-day period, from Jan 1 to Dec 31, that does not to exceed 9 ppm-hrs in more than 2 years out of every 5 year period. Such an index would protect up to 69% of the trees evaluated by Lee et al. (2022) and would also keep most RYL for crops at 5% or below.

3. What are the Panel's views regarding the areas for additional research identified in section 4.6? Are there additional areas that should be highlighted?

EPA does a good job of reviewing the uncertainties that remain concerning the effects of O_3 on vegetation and ecosystems and it also provides a comprehensive list of research needs. However, EPA does not make any statements about whether these research needs require the establishment of new initiatives or how researchers might obtain funding to accomplish these goals.

Missing from this section is explicit acknowledgement that climate change has the potential to alter the RBL and RYL relationships reported in the PA. It should be noted that most of the relationships analyzed in the PA were completed when EPA and other agencies were funding such research, some 25-35 years ago. At that time (mid 1980s to mid-1990s) atmospheric CO_2 concentrations were 50-70 ppm lower than today (latest estimate from the Mauna Loa site is that atmospheric CO_2 is now 420 ppm: https://gml.noaa.gov/ccgg/trends/ - accessed 3-23-23).

Data from the Aspen-FACE site in Wisconsin showed that elevated CO_2 moderated the response of several tree species to O_3. Since CO_2 is rising at ~2 ppm/yr, by 2050 it could be ~480 ppm, which is 1.7x higher than pre-industrial concentrations (assuming 280 ppm). Such high CO_2 concentrations will no doubt impact exposure-response relationships, as may rising temperatures, and EPA should be considering supporting new research in this area to update the RBL and RYL relationships, so they reflect potential future climatic changes.

In addition, EPA has stated that more research is necessary with regard to plant-insect interactions before it can determine if there are responses that would force a reconsideration of the current secondary standard. These research efforts too, should take into consideration rising CO_2, and associated climatic changes, such as elevated temperatures.

Dr. Jennifer Peel

Chapter 3 – Review of the Primary Standard

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?

- In general Chapter 3 is very well written and organized and represents an enormous amount of effort by EPA
- The approach with a focus on evidence from controlled human exposure studies is clearly described and acknowledges important limitations of evidence from these studies
- The choice to not include the epidemiology studies in the considerations in this chapter is not well-justified. My understanding is that this choice was made because none of the epidemiologic studies considered has a design value that is lower than the current standard.
- To inform the target level, the form of the standard, and its relevance to protect health with an adequate margin of safety, we also want to ask the question about ambient concentrations at which we observe adverse health effects, including in the most at-risk populations
- Regardless of the design value for measured concentrations included in an epidemiologic study, we can learn from these studies about whether we observe adverse health effects at ambient concentrations below the regulatory standard, e.g., Strickland et al.2010; we cannot assume that observed health effects would go away if the areas had met the standard, as the bulk of the observations driving the associations are likely meeting the standard. We can also learn about populations at higher risk. Evidence to support observed associations along the range of concentrations is presented in the 2020 ISA Figures 3-9, 3-10, 3-11.
- From the 2020 ISA, Table IS-4, describing evidence for short term respiratory ED/HA also provides evidence that health effects are observable a lower concentrations: " Evidence from many recent, large multicity epidemiologic studies provide further support for an association between ozone and ED visits and hospital admissions for asthma; associations are generally strongest in magnitude for children between the ages of 5 and 18 years in studies with mean 8-h daily max ozone concentrations between 31 and 54 ppb. Additional epidemiologic evidence for associations between ozone and hospital admissions and ED visits for combinations of respiratory diseases (31 to 50 ppb as the study mean 8-h daily max), ED visits for COPD (33 to 55 ppb as the study mean daily 1-h max), and ED visits for respiratory infection (33 to 55 ppb as the study mean daily 1-h max)."
- From the same table in the ISA: "Recent epidemiologic evidence for respiratory mortality is limited, but there remains evidence of consistent, positive associations, specifically in the summer months, with mean daily 8-h max ozone concentrations between 8.7 and 63 ppb. When recent evidence is considered in the context of the larger number of studies evaluated

in the 2013 Ozone ISA, there remains consistent evidence of an association between short-term ozone exposure and respiratory mortality."

- Similar information for long term exposure and health is presented in Table IS-5 from the ISA
- An additional key consideration from the epidemiologic evidence is that a lower threshold for health effects are not observable does not exist, or if it does it is likely at low levels below ambient concentrations in real-world settings.

2. In the Panel's view, does the discussion in section 3.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current primary standard and associated considerations regarding conclusions on a range of supported levels?

- Use of ozone as the indictor is well-justified given the lack of data and evidence for other indicators.
- May want to consider if there is evidence to support the 8-hour average form (as opposed to the 1-hour max or other forms) outside of the older human controlled exposure studies evaluating 6-8 hour exposures. Similarly, the form of the standard is not well-justified in the current draft
- I do not agree with the EPA's conclusion that the existing standards are protective; I came to this conclusion because of the lack of consideration of the epidemiologic evidence as well as the lack of extrapolation of evidence to the populations at highest risk, including children (not only at summer camps, but all children who spend time outside and/or in settings where exposure to ozone occurs), outdoor workers, asthmatics, and others with underlying respiratory conditions.
- Given the evidence presented in the ISA and the PA, EPA should consider target levels down to 50ppb, at a minimum down to 60ppb
- Approach to exceedances due to exceptional events could be reconsidered given the influence of wildfire events

Other sections:

- On page 2-33, the section about wildland fires may be outdated given recent trends, particularly in the Western US and particularly with earlier fire seasons experienced in many parts of the US.
- Chapter 2: intra-urban (within city) and other finer spatial variability is not well-described; would we expect to see variability not captured by the existing ozone monitors?

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Dr. Richard E. Peltier

Chapter 3 – Review of the Primary Standard

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?

In general, the PA is written to a high scholarly caliber, well-organized, and is viewed as a comprehensive document. There are some areas that appear somewhat repetitive, but this does not warrant additional work. I would strongly recommend, given its length, that the EPA consider the use of a table of contents to better facilitate public engagement.

In my view, the synthesis and approach in considering the health effects evidence presented by the ISA are generally sound. However, I remain concerned that the ISA relied on a PECOS tool that was unnecessarily restrictive in what science was permitted for review. I do recognize that the ISA is not subject to further revision, however. The pool of evidence on health impacts from ozone could, and should, be much deeper, and it is clear there is extensive evidence in both experimental and epidemiological literature where, had they been included, the conclusions at the lowest exposure concentrations would be less uncertain. This is also a point raised by members of CASAC and the public. As a result, I view the current PA as somewhat less comprehensive than if additional evidence had been considered.

In this light, and absent excluded evidence, it does lead to reasonable questions regarding the confidence that EPA expresses in assessing risk, which strongly (and in my view, wrongly) concludes that there is little reason to reconsider the primary standard. I'm not as confident that this is the correct decision for several reasons:

1. The body of literature, including both those falling within and outside the scope of PECOS, indicates important health impacts at levels below 70ppb.There is limited but clearly present evidence observing important health risks at less-than 70 ppb ozone exposures, including decreased lung function (Adams, 2002, Brown, 2008, and Kim, 2011) and airway inflammation (Kim, 2011), all occurring at 60-63 ppb using CHE approaches. The inclusion of causal relationships between long- and short-term ozone exposure and metabolic effects needs further context and evidence, but warrants additional caution be taken.
2. There remains an appearance of preference to drive recommendations based heavily upon CHE results, which describe the most compelling evidence for health impact at 70+ ppb exposures. While these are convincing results, they generally do not assess impacts to

susceptible populations, such as for children and/or asthmatics (noted in this PA, P3-84, line 23), nor can they currently inform on multipollutant exposures. In my view, they should represent only an upper bound to the primary standard consideration.

3. Modelled risk for exposures at one- or two/four-or-more-day exposures (described in Table 3-6 through 3-10) across different scenarios (elevated respiration, different lung function decrements, etc) are discussed in the text as simple percentages. Table 3-6 and 3-8 also provide useful additional context by also including estimated numbers of individuals, though they are not generally discussed in the text. At 60ppb, some 15-70k children will be exposed to ozone at one or more days in a year. At 70ppb, an estimated 727-8,305 children will be exposed to one or more days in a year. Additional estimates of exposures are similarly provided in Table 3-8. Given that there have been long-standing recommendations that the standard be set between 60-70ppb for a number of prior recommendations, and there is likely to be further disagreement on where the standard should be set in this PA review, it is important to recognize that large numbers of children are likely to be exposed to ozone, and this will continue to occur until communities reach attainment for the standard. Nonetheless, there remains a large, vulnerable population at risk for these exposures. It is important that this number be considered when informing the Administrator on an adequate margin of safety.
4. Much of the reviewed epidemiological work occurred in regions that exceeded standards and the EPA concedes ‘the extent to which these [included] studies can inform identification of exposure concentrations likely to elicit health outcomes under air quality conditions meeting the current standard is limited”, based on PA 3.3.3 and presented to CASAC on 02 March 2023. This suggests that the available epidemiological evidence is of insufficient quality to inform on a standard below 70 ppb because it is too polluted to be useful. As such, we are led to a constrained conclusion that with the limited data we can use, and knowing that EPA cannot consider other studies (where ozone concentrations might be lower) because of PECOS criterion limitations, we have effectively no available epidemiology to guide a standard determination below 70 ppb. Aside from supporting causality determinations (which has been reaffirmed a number of times), it is not clear why EPA considers, and then discounts, this line of evidence, without seeking additional epidemiological evidence to further reduce uncertainty around development of a standard. As a result, much uncertainty remains and the recommended approach (to retain) is not a precautionary one.

3. What are the Panel’s views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

The recommendations for additional and needed research are generally comprehensive, and would do much to reducing existing uncertainties that remain towards understanding ozone health impacts. To me, there are three main thrusts in which EPA can foster additional research:

1) Identification of methodologies to reduce exposure misclassification and bias that exists between the use of central monitors and actual exposures. While personal exposure assessments are likely to be the most precise and accurate measure, they are also viewed as the more challenging and complex approaches to take. EPA should consider work centered on model fusion approaches that improve spatial granularity, increase more diverse microenvironmental monitoring as assess breadth of exposures, and aim towards a specific focus on the most vulnerable populations, such as specific communities with disproportional prevalence of asthma, or in areas where ozone is likely to frequently impact children and/or outdoor workers. This would improve both exposure and risk assessment, and provide additional epidemiology results into the literature.
2) While controlled human exposure studies have revealed substantial knowledge about ozone exposures and health impacts, much uncertainty remains, particularly given that co-pollutants are typically absent in these studies which may play a determinative role in disease mechanisms and clinical and subclinical responses. At present, co-pollutant impacts are largely undescribed in CHE studies. EPA might consider supporting research to better mimic ambient conditions within these CHE projects, including the introduction of co-pollutants though techniques such as concentrated ambient particles along with, or without, ozone concentrations in the 40-70 ppb ranges.

EPA notes the potential value of using low-cost sensors (LCS) for ozone monitoring which, if successful, will facilitate better exposure monitoring in additional locations (i.e. point #1, above). However, LCS monitor performance for ozone and related photochemical oxidants remain fairly uncertain, particularly at typical ambient concentrations, with most LCS research to date focusing on measurements of particulate matter size fractions, including instrument characterization and performance testing. In order to use LCS to quantitatively assess ozone, EPA should first support the development of improved LCS techniques for ozone detection, rather than deploying still-uncertain LCS to increase ozone concentration data availability.

Dr. Alexandra Ponette-González

Chapter 4 – Review of the Secondary Standard

1. What are the Panel's views on the approach to considering the evidence for welfare effects and quantitative air quality/exposure analyses to inform preliminary conclusions on the secondary standard?

- The policy assessment relies on the existing body of scientific evidence and technical information. The assessment includes: (1) a summary of the available and *newly* available scientific evidence for ozone (O_3) impacts on vegetation and ecosystems, (2) a description of the various effects that could constitute public welfare effects, (3) supporting quantitative air quality and exposure analyses, and (4) a discussion of uncertainties and limitations in the scientific assessment. This general approach is both sound and effective.

- The assessment reviews the various categories of O_3 effects across levels of organization, from plants to ecosystems: visible foliar injury, whole plant effects, plant-insect interactions, ecosystem level effects (e.g., ecosystem productivity, biogeochemical and water cycling, community composition) etc. Effects on climate are also addressed.

- Emphasis is placed on those effects for which the evidence base is strongest, in this instance effects on plant growth (i.e., relative biomass loss and relative yield loss) observed in experiments conducted with tree seedlings and crops. For each category, new evidence is reviewed, and the extent to which it is consistent with or expands on previous findings is considered.

- Regarding public welfare effects, the types of O_3 impacts that could affect or are relevant to public welfare are clearly outlined and whether the evidence can be used to support clear conclusions about public welfare effects is considered.

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?

- The evaluation of the available information is sound with regards to certain categories of effects, and for the most part the evaluation is clearly communicated.

- Given the extensive amount of information presented, the complicated history of the secondary standard, and the existing uncertainties and limitations, there are areas in the document where a few additional tables and figures would improve clarity.

- The detailed background section was useful but given the nature of the history, sometimes hard to follow. A summary timeline of key events and outcomes would be helpful here.
- A summary table of the newly available evidence, its link to or implication for public welfare effects, or alternatively a summary list of major points would also be helpful at the end of section 4.3.

- In Section 4.3, the associated limitations and uncertainties section was strong. The policy assessment underscores that decades of evidence clearly demonstrate O_3 impacts on vegetation and ecosystems, but whether and how the science can inform public welfare effects is more difficult due to the various limitations associated with existing scientific studies (e.g., experimental design), modifying factors (e.g., meteorology), and how impacts may be distributed across groups (e.g., effects on consumers vs producers).

    - It is unclear why the limitations and uncertainties inherent in our understanding of the public welfare effects of O_3 on impacts on crops are greater than those for trees. Is the human aspect of crop management what leads to greater uncertainty with regards to public welfare effects. Is this the justification for not considering crop yield loss in more depth?

- Regarding median RBL and RYL values, losses can be considerably higher than 6% depending on the species and crop. Using a median value to characterize the wide range of losses experienced by trees and crops is not appropriate.
    - In the case of crops, 5 of 10 crops species have 7.5% or higher yield losses. Cotton, soy, wheat are among the crop species with the highest losses, and among the most important in the US in terms of cash crop production. Combined, these crops represent 30% of US cash crop receipts.

- In Section 4.4, the air quality and exposure analyses are clearly explained.

- Note: On page 4-66, the text states:

  "It can also be seen that there are some sites that have relatively lower W126 index values, e.g., less than or equal to 13 ppm-hrs in the Northwest, Northeast and Midwest, while recording N100 or D100 values of more than 5 (including some values above 10 and 5, respectively."

- However, on the maps it is difficult to discern where the N100 and D100 values above 5 in the Northwest and Midwest are located. Perhaps these sites could be indicated with an arrow or a circle.

- The air quality and exposure analyses provide evidence for the current secondary standard controlling cumulative seasonal exposures and peak concentrations. Relationships between design values and the W126 index show good correlations across regions, although there is much more scatter in the annual relationship.

- For peak, concentrations, the annual W126 index only approaches the current standard in terms of limiting the number of hours with peak concentrations and number of days with such hours at a value of 7 ppm-hrs.

- The air quality and exposure analyses provide evidence for the current secondary standard controlling peak concentrations.

- Interestingly, Table 4-1 suggests that an annual 4th max value (annual 4th highest daily maximum 8-hour average O_3 concentration) is more effective than a 3-year 4^{th} max value in controlling peak concentrations. The table also shows that for a W126 value to have a similar effect on peak concentrations, this would need to be at a level of W126 < 7 ppm-hours.

- The PA underscores the role of both cumulative seasonal exposures and peak concentrations in affecting vegetation and argues that the current standard can encompass both.

- The crux of the issue is whether a median RBL or RYL value is sufficient to provide the requisite level of protection for a broad representation of plants.

2. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

- Section 4.5 considers the welfare effects evidence related to O_3, the approach used to assess the adequacy of the secondary standard for protecting public welfare, and findings from the additional air quality and exposure analyses.

- The discussion provides rationale to support staff conclusions that the current secondary standard offers adequate public welfare protection.

- The discussion makes the following points:
    - O_3 is the most important photochemical oxidant and serves as an indicator for all photochemical oxidants, with no new literature demonstrating the contrary.

- The assessment is primarily based on vegetation-related effects of ozone, for which the evidenced is strongest and causal, rather than categories with expanded but unclear evidence (e.g., plant-insect interactions), or climate effects for which the uncertainties of O_3 impact at regional scales within the US remain too large.
- New studies on growth effects that encompass the range of O_3 exposures associated with the current standard are not available, meaning that it is not possible to predict effects on tree growth where air quality meets the current standard.
- The W126 index does not capture the effects of peak concentration patterns that affect vegetation.
- Other quantitative relationships between vegetation effects, such as visible foliar injury and O_3 are not adequate for assessing this category of effect under different air quality conditions.

- For the most part, this section of the document supports the notion that the current standard is sufficient to protect against adverse public welfare effects, including those associated with visible foliar injury.

- However, in considering use of W126 index in a single year or three-year average, only the evidence pertaining to tree seedlings is considered. More discussion on how this would apply to crops is warranted. For annual crops, the question is whether a 3-year average would ensure protection.
  - The document states that "single-year W126 index values generally to vary by less than 5 ppm-hrs from the 3-year average when the 3-year average is below 20 ppm-hrs)." Under these circumstances, both crops and seedlings can still incur significant biomass and yield losses in any given year. For trees, these effects compound over time and should be considered.

- The document states that there are "complexities associated with identifying adverse public welfare effects for market-traded goods (where producers and consumers may be impacted differently)"
  - Presumably, producers are impacted in terms of income while consumers are impacted in terms of food and food prices. Are there other impacts might be incurred on the producer side that need to be considered?

- Regarding potential alternative options, the EPA states the following: "Accordingly, we conclude it is important to consider both a cumulative exposure metric, such as W126 index, and a peak exposure metric in assessing air quality with regard to the potential for specific exposure conditions that might be harmful to vegetation."

    - Missing in this analysis is how the current secondary standard compares to such a potential alternative comprised of a cumulative seasonal exposure metric and hourly concentration metric.

3. What are the Panel's views regarding the areas for additional research identified in section 4.6? Are there additional areas that should be highlighted?

- The list of areas identified stems from the assessment of uncertainties and limitations in scientific and technical information and addresses several knowledge gaps that preclude bridging the gap between scientific evidence and protection of public welfare effects. Even so, there are additional areas of research that could be highlighted.

- Additional research needs to be conducted on public experiences and perceptions of pollution impacts on vegetation and ecosystems. What conditions lead the public to experience an area as O_3-affected or impacted, and how does this vary across space and time? What circumstances diminish the public's enjoyment of landscapes, including Class 1 areas?

- As wildfire regimes continue to change, more plant experiments and observations that account for/consider peak O_3 concentrations associated with wildfire episodes will be important, especially for those regions, such as the Western and Southwestern US where many sites often do not meet the current air quality standard.

- Additional research is needed on the key climate changes that can and will modify the relationship between O_3 and vegetation. For example, changes in CO_2 can lead to decreased stomatal density and stomatal closure, reducing O_3 uptake and in turn leading to lower O_3 impact on crop yields (see Leung et al. 2022, Tai et al. 2021).

- Given the well-documented effects of O_3 on crop yields, further research should also address/consider those aspects of management that may exacerbate or mitigate O_3 effects on crops.

<u>Minor Comments</u>

- Page 4-27, sentence repeated
    - Uses or services provided by areas that have been afforded special protection can flow in part or entirely from the vegetation that grows there.

- Page 4-20, "agency" repeated
- Page 4-85, change "*although does not provide for identification" to "but does not…"*
- Page 4-92, extra period after (Frey, 2014).

References

Leung, F., Sitch, S., Tai, A. P., Wiltshire, A. J., Gornall, J. L., Folberth, G. A., & Unger, N. (2022). CO2 fertilization of crops offsets yield losses due to future surface ozone damage and climate change. Environmental Research Letters, 17(7), 074007.

Tai, A. P., Sadiq, M., Pang, J. Y., Yung, D. H., & Feng, Z. (2021). Impacts of surface ozone pollution on global crop yields: comparing different ozone exposure metrics and incorporating co-effects of CO2. Frontiers in Sustainable Food Systems, 5, 534616.

Dr. Jeremy Sarnat

Chapter 3 – Review of the Primary Standard

In general, I found Chapter 3 of the draft ozone Policy Assessment to be clear and well-written. I appreciate the tremendous effort and attention to detail that EPA staff put into this assessment, which is evident throughout this draft document. Below are my specific comments and questions addressing Charge Questions 1 and 3.

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?

- **Interpreting the epidemiologic findings**. There is a strong tendency throughout the PA to dismiss the weight of the epidemiologic evidence, relative to the smaller number of human controlled exposures studies, given both the lack of epidemiologic control for potential co-pollutant confounding and derived design values in the epi studies exceeding the NAAQS. (See comment above concerning sensitivity around the design values with varying the ozone NAAQS form). My feeling is that there needs to be a reconsideration of how observational studies inform the PA, if not for the current PA, then for future ISA cycles (for ozone and the other criteria pollutants).

  I believe the preponderance of studies showing positive, significant observations with ambient ozone in cities with varying ozone distributions, population demographics, and factors modifying exposures to ozone is too great to diminish. Epidemiologic evidence, collectively, should not be deemed less relevant to the HREA process due to derived design values exceeding benchmarks.

  I encourage EPA staff and their colleagues to consider novel approaches for reanalyzing historic single-city epidemiological data, potentially using truncated distributions or observations censored to include days below the benchmark concentrations. Similarly, meta or combined analyses might be useful to focus on the shape of C-R curve at parts of the exposure distribution more relevant to the NAAQS benchmark level.

  This comment is consistent with recommendations from the 2022 NAS panel, '*Advancing the Framework for Assessing Causality of Health and Welfare Effects to Inform National Ambient Air Quality Standard Reviews*' urging EPA to look into emerging research methods, which include advanced methods for controlling for confounding, the use of novel causal inference techniques, joint effects modeling, and the application of untargeted, highly-multidimensional data in establishing causal inference through machine learning methods. While methodologically novel and potentially challenging, my overarching sense is that not enough is currently being done to fully interrogate and learn from the epidemiologic lines of evidence.

- **Lack of controlled data around 70 ppb**. The use of controlled human exposure findings is, for the case of the ozone PA, warranted. Despite this, it is worth highlighting the relative lack of studies examining exposures at or around a 70 ppb target concentration (with Schelegle 2009, being the exception). Although the collective body of results from the chamber studies are indicative of a linear or near-linear C-R relationship, the paucity of actual, empirical observations around a 70 ppb benchmark is a source of potentially consequential uncertainty and one that weakens the risk assessment, especially given the weight assigned to this line of evidence.

- **Robustness of the ozone NAAQS form**. Among the key ozone NAAQS elements, I have several questions concerning its form. While the 1997 decision to adopt a concentration-based form over one that is exceedance- or percentile-based is reasonable, the use of the 4th highest annual 8h moving average over a 3-year period seems somewhat arbitrary. Page 3-6 of the current PA notes that:

  > *With regard to a specific concentration based form, the fourth-highest daily maximum was selected in 1997, recognizing that a less restrictive form (e.g., fifth highest) would allow a larger percentage of sites to experience O3 peaks above the level of the standard, and would allow more days on which the level of the standard may be exceeded when the site attains the standard (62 FR 38868-38873, July 18,1997), and there was not a basis identified for selection of a more restrictive form (62 FR 38856, July 18, 1997).*

  I think it would be useful to present sensitivity analyses around this aspect of the form (either relaxing or making it more restrictive), especially as it relates to:

    - The number of days, across the US, where the standard would be exceeded under different forms;
    - How a slightly changed form would affect the comparison-to-benchmark analyses; and
    - How the corresponding assessment of attainment in the cities where the epidemiologic analyses were conducted.

- **Revisions to APEX input parameters**. Page 3-70 of the draft PA differences in the modeling parameters in the 2015 and 2020 exposure assessment. An area of reconsideration should be exposure factors related to building infiltration, related ventilation factors (i.e., prevailing indoor-outdoor penetration rate by locale), and human behavioral response to climate-related change. These rapidly changing exposure factors may serve to reduce or increase ambient ozone exposures across populations. It was not clear, however, if these model inputs were unchanged when conducting the most recent APEX modeling. Although noted as a potential area of future research, inputs on human activity patterns used in APEX and other exposure models are likely dated and in need of revision.

- **Communication around absolute risk**. Relatively minor point, but I prefer, from a risk communication standpoint, presenting total *number of individuals* experiencing lung functions decrements as the primary health risk indicator, rather than *percentages* of the population affected (as illustrated in Table 3-11). I believe that the absolute numbers provide a more comprehensible message regarding potential risk under different benchmark exposure scenarios. These numbers are available (subset presented in Table 3-8; and in Appendices 3D 40-62), but get a bit lost in the other health risk indicators.

3. What are the Panel's views regarding the areas for additional research identified in section 3.6? Are there additional areas that should be highlighted?

- Since most of the controlled studies cited in the 2020 PA were conducted, new omics-based methods have emerged to identify molecular-level response to oxidant exposures, which may offer added strength of evidence regarding the causal determination, susceptibility and inter-individual heterogeneity in ozone exposure and response. These methods have been used in panel study designs, as well, and would be suitable for use in studies of individuals spending greater frequencies outdoors, including children's summer camp and adult outdoor occupational settings.

- The draft Policy Assessment rightly focuses on children and adults with asthma as two key at-populations. Although the ISA and parts of the draft PA rightly note that ozone exposure disparities associated with sociodemographic vulnerability, future assessments should consider including low-SES and specific communities of color as also being potentially at-risk and disparities in ozone exposure as being an understudied case involving environmental equity. I would like to see future assessments focus on modeling exposures for these communities as part of the HREA process. Research to facilitate these models should be pursued and supported.

- Broadly, it seems like exposures modeling for applications such as an ISA Policy Assessment should consider behavioral response to varying pollutant concentrations, including response to public health messaging regarding individual-level response (i.e., AQI messaging). This aspect of air quality health messaging and its impact on corresponding human exposure (and societal burden associated with this response) has become clearer following public health messaging around both the covid pandemic and the increased forest fires in the western US, where many individuals change their time-activity and lifestyle patterns in response to perceived risk.

Put differently, there are additional health-related impacts born largely by individuals at-risk from elevated ozone associated with the response of these individuals to avoid what they perceive as risky behavior (i.e., going outdoors, engaged in physical activities). How do we measure or model these impacts? Is it possible to gauge how the NAAQS setting process affects these behaviors?

Dr. Jason West

Chapter 2 – Air Quality

1. To what extent does the Panel find that the information in Chapter 2 is clearly presented and that it provides useful context for the reconsideration?

Chapter 2 provides background information that is clearly presented, and provides useful context for the reconsideration, with some comments to follow.

As I understand, the purpose of the Policy Assessment is to draw out information from the Integrated Science Assessment that is most relevant for policy and decision-making for setting the standard. In this context, this chapter seems quite long and detailed to me, though the content provided is good quality. Several figures on ozone levels and trends are updated from the ISA, given the fact that the PA is now being rewritten based on the 2020 ISA, and those updates are appropriate and helpful. The long section on background ozone (USB) seems out of place given that what is written here is longer than what appeared in Appendix 1 of the 2020 ISA, and Page 2-28, line 5 says "The section, which presents the information and analysis that were also presented in the parallel section of the 2020 PA." It would be better to state how this review differs from the 2020 PA. Later it seems that the purpose is to present new USB O3 estimates, but that is not clear at the start of this section. EPA may have reasons to write this long section, but to me it seems out of proportion given what I understand to the be purpose of the PA. The USB analysis focuses on MDA8 as a health-relevant metric, but I don't see that metrics relevant for plants are also modeled (perhaps that was beyond EPA's capability), and so that may be a limitation in considering the secondary standard.

While section 2.5.4 presents a nice summary of the findings from the new USB analysis, the section does not present or discuss how USB is relevant for the decisions in setting the primary or secondary ozone NAAQS. Searching the document for "USB" I see that it is not used once in Chapters 3 or 4. If USB is not used in EPA's analysis of primary and secondary NAAQS values for the Administrator, then why is it important to have this in the PA? I do not wish to argue that it is not relevant, but that EPA should consider being explicit about how USB might be used in setting NAAQS and what is their motivation for including this analysis in the PA.

For future PAs, EPA could consider whether it is important to repeat technical discussions from the ISA as background, and whether PAs might more effectively draw out background information from the ISA for supporting policy recommendations for the NAAQS.

Figure 2-1 presents emissions from the NEI for ozone precursors. For NOx, VOCs, and CO, biogenic emissions are clearly presented as a wedge of the pie chart. The CH4 plot does not list biogenics. I'm aware that biogenic emissions are a major source of emissions globally, but I'm not sure in the US. Are biogenics included in the "Other" category for CH4? Or if biogenic CH4 are excluded from this pie chart, then the caption should explain that is the case.

Page 2-17, l. 5 or caption for Figure 2-9 – The level of significance in the trends should be stated (p-value or equivalent). EPA should be aware that statisticians encourage moving away from statements of significant or not significant and toward reporting p-values and using calibrated language like "very likely" etc.

Page 2-17, l. 9 – Would it be worth mentioning changes in electricity generation, particularly closing of coal-fired power plants, as a cause for the ozone decreases?

Page 2-35, l. 24 – To me, "Post-Industrial" means after industrial activities stop, or when services outweigh heavy industries. I don't think that is the intention here. How about "Industrial Methane" or "Human-caused Methane" or "Methane Increases since the Industrial Revolution". The term post-industrial is also used later in this section.

Page 2-35, l. 28 – I don't think it's correct to say that fossil fuel combustion is a major source of methane. Fossil fuel extraction and use (coal, oil and gas) are a major source. I think it would be better here to just list all major anthropogenic sources.

Page 2-36, line 9 – "A major limitation with existing model-based estimates of the influence of global methane on current U.S. O3 concentrations is our limited understanding of historical methane emissions." I don't think this is a major limitation. For methane, it is concentrations rather than emissions that directly determine contributions to ozone, and methane concentrations from well before the Industrial Revolution are known from ice core samples. The preindustrial contribution of methane to O3 is constrained by the preindustrial CH4 concentration, which is presumably a result of mainly natural emissions with small anthropogenic contributions. Perhaps instead EPA could discuss here how methane's contribution to USB O3 is a result of anthropogenic methane emissions from the US and all other nations, and that the US contribution is usually not separated.

Page 2-36, line 32 – Is this saying that HTAP emissions have more direct contributions from individual countries than CEDS or EDGAR? I don't think this is true. I also am not sure that national emissions estimates are more accurate than international ones.

Section 2.5.1.7 – I'm not clear on why this section omits carbon monoxide (CO). Much of what is said here would also apply to CO.

p. 2-38, line 20 – I'm not clear why CO is omitted from these emissions. And when EPA says methane is omitted, I assume that is for estimating domestic contributions. Foreign contributions should include methane.

Figure 2-19 – I think what is shown is the 3-month average of MDA8.

Figure 2-30 – I think this is showing MDA8 ozone concentrations, and that should be stated in the figure caption.

Chapter 4 – Review of the Secondary Standard

1. In the Panel's view, does the discussion in section 4.5 provide an appropriate and sufficient rationale to support staff's preliminary conclusions with respect to the current secondary standard and associated considerations regarding conclusions on potential alternative options?

The PA dismisses effects of tropospheric ozone on climate as a basis for a secondary ozone standard, because of the difficulty and uncertainty in relating ground-level concentrations over the US with global climate effects. I think the EPA is right to do this, as a concentration-based standard is perhaps not a clear way of addressing ozone's influence on climate under the Clean Air Act. But my sense is that the argument for why it is dismissed is not clearly laid out.

On p. 4-63/64, EPA states that ozone's influences on climate are more uncertain than that of other greenhouse gases. While this is true, we do have a good ability to quantify ozone's radiative forcing and impacts on climate, and EPA does not evaluate whether this quantification is sufficiently certain to consider it further as a secondary standard. This paragraph cites uncertainties, but these are not the same uncertainties that are given as the reason for discounting ozone's climate influences in Section 4.5.2.

Later Section 4.5.2 (page 4-119) cites "limitations and uncertainties in the evidence base that affect our ability to characterize the extent of any relationships between O3 concentrations in ambient air in the US and climate-related effects". And later a "lack of quantitative tools". While this is true, it is also true that O3 is known to be a greenhouse gas and that concentrations in air above the US are contributing to global warming, which we observe to be happening due to human emissions (IPCC, 2021), and the contribution of global tropospheric ozone has been quantified. Current global models, while uncertain, have been used to quantify the contribution of emissions from North America (if not the US) to global ozone radiative forcing and global temperature change. Current global models also can consider the effects of reducing O3 concentrations only over the US (however that might be done), even if exactly this experiment has not been conducted. So I'm not sure model insufficiency is the problem. But this paragraph gives a better articulation for excluding ozone on climate than on 4-63.

I agree that it would be difficult to establish an ozone concentration over the US that would protect public welfare from damages of climate change. But to me, the reasons why include these:

- O3 concentrations through the troposphere affect climate, not just at ground level.
- Climate change is a global phenomenon with global drivers, not just O3 concentrations over one nation.
- O3 is one of many GHGs or forcing agents contributing to global climate change, although the contributions of global O3 have been quantified.
- While NAAQS intends to ensure concentrations do not exceed standards at any particular location or time, it is the net effect of all elevated (above natural background) O3 levels that affects climate warming, not peak concentrations.
- Emissions of ozone precursors influence both methane and ozone concentrations, and how ozone is controlled determines the effects of those controls on climate.

I would encourage EPA to consider a broader discussion of these factors, as the logic for excluding ozone.

On the last point, the PA does not discuss the relationships between emissions of precursors – NOx, VOCs, CO and CH4 – on ozone radiative forcing and climate impacts. Briefly, reducing VOCs, CO and CH4 benefit climate by reducing both ozone and methane concentrations, while reducing NOx alone is generally thought not to benefit climate because the resulting increase in methane outweighs the reduction in ozone in climate forcing. How ozone concentrations are reduced therefore determines the climate impact, not just the ozone concentration, which is what the NAAQS regulates. Discussing these relationships can strengthen the case for why EPA chooses not to pursue a secondary NAAQS further for ozone's effects on climate, because it would show that setting a standard for ground-level ozone concentration over the US may not effectively slow climate warming. This CASAC's review of the 2020 ISA suggested that EPA consider adding this discussion to future ozone ISAs, and here I'd suggest some discussion of these choices for the NAAQS. Doing so could clarify whether reducing uncertainties and improving tools might make ozone's effects on climate a basis for a secondary NAAQS in the future. It could also further clarify and motivate EPA actions apart from the NAAQS process that would benefit climate change by encouraging reductions in US VOC, CO and CH4 emissions.

p. 4-25 bottom – I suggest 3 short additions to this paragraph. 1) Acknowledge that tropospheric ozone's impacts on climate result from global concentrations through the depth of the troposphere, and not just ground level concentrations. 2) I suggest adding a sentence to discuss how ozone impacts on global vegetation impacts the carbon cycle. 3) The statements about ozone's importance for climate are based on the 2020 ISA. These statements are broadly consistent with findings in the IPCC AR6, which came out after the 2020 ISA, and so this sentence could reference finding from the AR6.

p. 4-30 middle – Consider saying more about the negative impacts of climate change (and ozone's contributions to it), rather than immediately discounting it because of uncertainties with relationships between ground-level concentrations in the US and climate effects.

In light of this discussion, I would like to recommend that EPA consider outlining and discussing the ways in which the NAAQS would be a cumbersome or illogical way to address the impact of ozone on climate change, but I acknowledge that EPA may consider this discussion too broad for this document and may choose not to do so. Second, the document emphasizes uncertainties and lack of tools in the impacts of ozone on climate change to justify their choice not to suggest a secondary standard. I think that in fact we know a lot about the impacts of ozone on climate change, and so I would recommend that EPA be more precise about what is known well vs. the particular uncertainties they are referring to here regarding a secondary standard for ozone.

On crop yields, p. 4-130 states that "not every effect on crop yield will be judged adverse to public welfare". The section then explains that through crop management, yields can be maintained. These management actions include fertilizer. In this case, from an economic point of view, it would seem that if one doesn't account for the lost crop yields, then one should account for the cost of the excess fertilizer and environmental impacts from fertilizer application. I would think these impacts would be adverse to public welfare.

3. What are the Panel's views regarding the areas for additional research identified in section 4.6? Are there additional areas that should be highlighted?

This section is quite short, but the areas for future research are presented well. Given that the EPA finds uncertainty and lack of quantitative tools to be important in not suggesting a secondary standard for ozone's effects on climate, it might be appropriate to list some areas of research that would address these gaps. No comment is made here on investigating ozone's impacts on climate. From the discussion in earlier sections, it seems that EPA would benefit from applications of existing models that evaluate the radiative forcing and climate impacts of reductions in ground-level ozone over the US itself. Since no strategy would only reduce ground-level ozone, these studies could investigate the effects of reductions in ozone through the troposphere, or investigate emission reductions and their effects on ground-level ozone as well as radiative forcing and climate. Improvements in models would also be welcome, but it seems to me that the main limitation now is not the quality of the models but their application for these specific questions.