UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

February 19, 2020

EPA-CASAC-20-003

The Honorable Andrew R. Wheeler
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Subject: CASAC Review of the EPA's *Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards (External Review Draft – October 2019)*

Dear Administrator Wheeler:

The Chartered Clean Air Scientific Advisory Committee (CASAC) met on December 3-6, 2019, and on February 11-12, 2020, to peer review the EPA's *Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards (External Review Draft – October 2019)*, hereafter referred to as the Draft Ozone PA. The Chartered CASAC approved the report on February 12, 2020. The CASAC's consensus responses to the agency's charge questions and individual review comments from members of the CASAC are enclosed. Questions from CASAC members to a pool of non-CASAC member consultants and their responses are also enclosed. Major comments and recommendations are highlighted below and detailed in the consensus responses to charge questions.

The Draft Ozone PA depends on a Draft Ozone Integrated Science Assessment (ISA) that, as noted in the CASAC Report on the Draft Ozone ISA, does not provide a comprehensive, systematic assessment of the available science relevant to understanding the health impacts of changes in exposure to ozone, due largely to lack of a sufficiently comprehensive, systematic, accurate, and balanced review of relevant scientific literature; inadequate evidence and rationale for altered causal determinations; and a need for clearer discussion of causality and causal biological mechanisms and relevance to public health of the evidence presented. Given these limitations in the underlying science basis for policy recommendations, some CASAC members conclude that the Draft Ozone PA does not establish that new scientific evidence and data reasonably call into question the public health protection afforded by the current primary ozone standard. Other members of the CASAC agree with the previous CASAC's findings and recommendations in their review of the 2014 Second Draft Ozone PA. In that review, the previous CASAC opined that a primary standard set at 70 ppb may not be protective of public health with an adequate margin of safety. The CASAC also finds, in agreement with the EPA, that the available evidence does not reasonably call into question the adequacy of the current secondary ozone standard and concurs that it should be retained.

On overarching process issues, the CASAC strongly recommends that the EPA consider restoring a traditional interactive discussion process in which the CASAC can interact directly with external expert panels, while also keeping the option of obtaining written responses from external experts to specific questions. The CASAC strongly recommends that the EPA work with experts in causal analysis, biological causation, management science, decision analysis, and risk analysis to improve the causal determination framework. Experts from outside the air pollution health effects area should be included. The CASAC recommends that the EPA work with the National Academies to critically review and improve the logical and conceptual foundations for its causal analyses and the clarity with which its causal conclusions are expressed and communicated throughout the NAAQS review process and in the ISA and PA. The CASAC recommends that it be given an opportunity to review a second draft of the Ozone PA (with an updated Risk and Exposure Assessment) after the final ISA for ozone is released.

Turning to specific comments on chapters in the Draft Ozone PA, the CASAC finds that Chapter 1 gives a clear, although brief, discussion of legislative background and history that provides useful context for the review. For the final PA, the CASAC recommends that the EPA consider adding a discussion of the exceptional nature of the current CASAC and NAAQS review process. This could include: (a) further details of Administrator Pruitt's "Back to Basics" memorandum; (b) proceeding without an Ozone Review Panel and streamlining the review process to promote timely advice; and (c) appointing a pool of non-CASAC member consultants to expand the expertise and fields of knowledge used to inform the CASAC's review. The CASAC recommends several measures to more fully realize the Draft Ozone PA's stated goals of serving as a source of policy-relevant information, being understandable to a broad audience, and facilitating the CASAC's advice to the Agency and recommendations to the Administrator.

The CASAC finds the information in Chapter 2 to be clearly presented and useful as context for the review, but recommends adding discussions of how precursors contribute to ozone formation, and their relative importance, as well as differences in seasonality and trends within and between different regions of the United States. The treatment of ozone exposures related to wildfires and exceptional events should be expanded and clarified.

The CASAC has several specific recommendations, detailed in the attached report, for improving the accuracy, balance, comprehensiveness, and soundness of the material in Chapter 3. The CASAC recommends that the final ISA should provide a more balanced report of relevant epidemiology, to be reflected in the Final PA, as discussed further for the Draft Ozone ISA; causality determinations for metabolic effects should be updated to reflect the Final Ozone ISA; that FEV_1 decrements are not the only relevant health effect from ozone exposure should be more fully discussed, along with its implications for interpretation and application of the risk assessment results; and lack of empirical validation for risk modeling assumptions and predictions should be acknowledged and its implications for uncertainty about public health effects of changes in ozone exposures should be discussed. The CASAC recommends that a thorough quantitative uncertainty and variability analysis should be added and its implications for policy-relevant conclusions discussed.

The CASAC commends the EPA for the thorough discussion and rationale for the secondary standard in Chapter 4, and agrees with the EPA that the current secondary standard for ozone should be retained. However, the CASAC recommends that the Draft Ozone PA should more thoroughly address effects of ozone on climate change by providing quantitative estimates and uncertainty bands for effects of ozone on global warming and the consequence for economic and welfare effects on the United States.

The CASAC also has recommendations for future research needs, as detailed in the consensus responses to the charge questions.

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

Sincerely,

/s/

Dr. Louis Anthony Cox, Jr., Chair
Clean Air Scientific Advisory Committee

Enclosures

NOTICE

This report has been written as part of the activities of the EPA's Clean Air Scientific Advisory Committee (CASAC), a federal advisory committee independently chartered to provide extramural scientific information and advice to the Administrator and other officials of the EPA. The CASAC provides balanced, expert assessment of scientific matters related to issues and problems facing the agency. This report has not been reviewed for approval by the agency and, hence, the contents of this report do not represent the views and policies of the EPA, nor of other agencies within the Executive Branch of the federal government. In addition, any mention of trade names or commercial products does not constitute a recommendation for use. The CASAC reports are posted on the EPA website at: http://www.epa.gov/casac.

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

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Consensus Responses to Charge Questions on the EPA's
Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards
(External Review Draft – October 2019)

Chapter 1 - Introduction

Overarching Issues

The purpose of the Policy Assessment (PA) is to bridge the gap between the EPA's scientific assessments and the judgment required by the EPA Administrator when determining whether to retain or revise the National Ambient Air Quality Standards (NAAQS). It is unusual for the CASAC to review a draft PA and draft Integrated Science Assessment (ISA) simultaneously, insofar as the ISA provides the scientific basis for the PA. The CASAC recommends that it be given an opportunity to review a second draft of the Ozone PA (with an updated Risk and Exposure Assessment) after the final ISA for ozone is released.

As part of the current review cycle, the EPA provided the CASAC with a pool of non-CASAC member consultants who responded to written questions from the CASAC. Members of the CASAC found that this pool of consultants provided valuable insights and responses and useful information. However, the traditional review process, allowing interactive discussion between the CASAC and a pollutant-specific review panel, enables significantly more discussion and deliberation among experts with differing backgrounds and opinions, potentially resulting in a more comprehensive examination of some controversial topics. The CASAC strongly recommends that the EPA consider restoring this traditional interactive discussion process, while keeping the option of obtaining written responses from external experts in methodological and technical areas to specific questions from the CASAC, to complement the expertise of the review panel and reduce risks of groupthink, confirmation and conformation biases, and other biases that can impair group judgments and decisions.

A specific important technical area where the current NAAQS review process lacks adequate technical depth and clarity is its use of causal concepts and analyses to reach causal conclusions and to express them so that others (including expert readers) can clearly understand them. Although the causal determination framework in the draft ISA and PA for ozone has been endorsed for over a decade by previous CASACs, the current CASAC recommends that the causal determination framework be reevaluated with the goal of improving clarity and reducing ambiguity. Discussions with the EPA during the public meetings and written comments from some non-CASAC member consultants raise questions regarding the clarity of causal determination categories (please see Appendix B of the CASAC's Review of the Ozone ISA for further details). The CASAC therefore strongly recommends that the EPA work with experts in causal analysis, biological causation, management science, decision analysis, and risk analysis to revise and improve the current causal determination framework. Experts from outside the air pollution health effects area should be included. The CASAC recommends that the EPA work with the National Academies to critically review and improve the logical and conceptual foundations for its causal analyses and the clarity with which its causal conclusions are expressed and communicated throughout the NAAQS review process and in the ISA and PA.

Response to Charge Question

To what extent does the CASAC find that the information in Chapter 1 is clearly presented and that it provides useful context for the review?

The discussions of legislative background and history are clearly, although briefly, presented. They provide useful context for the review.

For the final PA, the CASAC recommends that the EPA consider adding a discussion of the exceptional nature of the current CASAC and NAAQS review process. Relevant background on changes in processes and procedures could include: (a) further details of Administrator Pruitt's "Back to Basics" memorandum (adding to the discussion on p. 1-12); (b) proceeding without an Ozone Review Panel and streamlining the review process to promote timely advice; and (c) appointment of a pool of non-CASAC member consultants to expand the expertise and fields of knowledge used to inform the CASAC's review.

Relevant background on methodological changes in the current CASAC's scientific and technical approach in this review cycle could be provided in a separate section. These changes should include stronger emphases on:

(1) Statistical association vs. biological (mechanistic) concepts of causation;
(2) Clarity and reproducibility of the evidence the EPA is using to draw conclusions;
(3) Emphasis on more effective integration of information from animal toxicology and controlled human exposure studies to:
    a. Elucidate and validate potential (i.e., hypothesized) causal biological mechanisms underlying epidemiologically suggested health risks; and
    b. Better characterize concentration-response (C-R) functions for pulmonary inflammation and other physiological responses to inhaled ozone.

The stated intentions for the Draft Ozone PA presented in Chapter 1 include "to serve as a source of policy-relevant information;" "to be understandable to a broad audience;" and "to facilitate advice to the Agency and recommendations to the Administrator" from the CASAC. The CASAC recommends that these intentions be more fully realized in the final Ozone PA by undertaking the following measures:

1. *Summarize available empirical evidence on how changes in public health effects depend on changes in ozone levels.* Ideally, this information should be discussed in detail in the final ISA.
2. *Accurately summarize final results from a systematic review and critical evaluation and synthesis of relevant studies relied on to reach conclusions*, including negative studies and studies of nonlinear C-R functions for ozone omitted in the draft ISA that should inform the PA. This review should be done in the ISA and summarized and referenced in the PA.
3. Throughout the Draft Ozone PA, *clearly distinguish between causal C-R functions (describing how public health risks change in response to changes in ambient ozone levels) and regression C-R functions* (describing how observed public health risks differ across different observed or estimated ambient ozone levels). In interpreting epidemiological data and models, the Draft Ozone PA addresses regression C-R functions and they should be defined as such and caveated appropriately.

4. *Discuss in more detail the health and policy implications of causal biological mechanisms of inflammation-related health effects in general and in sensitive populations,* including roles of inflammation in mediating adverse health effects, and implications of these mechanisms for causal C-R functions.
5. *Quantify uncertainty and variability in risk predictions, taking into account epistemic uncertainties (e.g., from model uncertainty and exposure estimation error) as well as sampling variability. Present comprehensive, quantitative uncertainty, sensitivity, and variability analyses showing how the PA's conclusions change for variations in modeling choices.*
6. *The Draft Ozone PA should more thoroughly address effects of ozone on climate change* by providing quantitative estimates and uncertainty bands for effects of ozone on global warming and consequences for economic and welfare effects on the United States.

Chapter 2 – Air Quality

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

Section 2.1 (O_3 and Photochemical Oxidants in the Atmosphere) should discuss how the precursor emissions listed in this section, oxides of nitrogen (NOx), volatile organic compounds (VOCs), carbon monoxide (CO), and methane (CH_4), are important for ozone formation. An overview of the chemical mechanisms should be presented, and important chemical reactions should be highlighted. The relative importance of each precursor should be discussed with respect to local (both urban and rural) ozone formation and transport (intrastate and interstate) and ozone formation in the remote troposphere. Also, the relative importance of NOx vs. VOCs should be discussed with respect to geographic location in the United States. (e.g., Southeast, Northeast, Central, Midwest, West).

Section 2.2 (Sources and Emissions of O_3 Precursors) presents estimated national values for 2014 National Emissions Inventory (NEI) emissions. However, there is no detailed discussion on the uncertainty associated with each pollutant or source sector. Some pollutants and sectors will be much more uncertain than others. For example, NOx emissions from electric generating units (EGUs) have low uncertainty since they are typically captured by hourly continuous emissions modeling (CEMs). On the other hand, other source sectors and pollutants may be highly uncertain. The uncertainties in the emissions inventory (magnitude, spatial allocation, and temporal allocation) should be discussed for each pollutant and source sector. In addition, it would be helpful to add national maps containing county-level emissions for NOx, VOCs, CO, and CH_4 to show the variability across the country. 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.

Section 2.4 (Ozone in Ambient Air) should include a discussion on ozone precursor trends in addition to ozone trends. Specifically, trends in NOx, VOCs, and CO measurements from national monitoring networks (AQS, near-road, NCore, and PAMS) should be included and discussed.

It is stated on page 2-19, "B shows the seasonal pattern for an urban site in Baton Rouge, LA. Throughout the southeastern U.S., the highest O_3 concentrations are often observed in April and May due to the onset of warm temperatures combined with abundant emissions of biogenic VOCs at the start of the growing season. This is often followed by lower concentrations during the summer months, which

is associated with high humidity levels that tend to suppress O_3 formation." Although this statement might be true for Baton Rouge, it does not apply to the entire southeastern United States. In addition, a reference should be provided to support the statement that high humidity levels suppress O_3 formation.

EPA's 2016 Exceptional Events Rule allows certain ozone measurements due to natural events to be excluded from the official design values when compared to the NAAQS. In some cases, identical exceptional events can be treated differently in one location vs. another based on how close the area is to the standard. In both locations, people could potentially be impacted by adverse health effects from ozone, but the data are removed in one location and not the other. The Draft Ozone PA should discuss how exceptional events are accounted for in the policy assessment.

Section 2.5 (Background O_3) describes the EPA's use of the Community Multiscale Air Quality (CMAQ) chemical transport model with the zero-out approach to estimate U.S. background, international, and natural contributions. Figures 2-22, 2-23, and 2-24 should add a 100% line. The EPA should add explanations for values over the 100% line. The caption in Figure 2-26 is incorrect. The figures and tables containing U.S. Background (USB) contribution on the average of the top 10 predicted O_3 days and the 4^{th} highest O_3 days are very useful and relevant to policy decisions. These values should be compared to previous work by Jaffe et al. (2018) and Parrish et al. (2017, 2019). In Appendix 2B, the scale used in Figure 2B-15 should be reduced from 100% to a lower value to allow the reader to see the differences between monitoring sites.

The EPA should consider extending the Photochemical Assessment Monitoring Stations (PAMS) monitoring season from 3 months (June, July, August) to 6 months (mid-April, May, June, July, August, September, mid-October) in ozone nonattainment areas since peak ozone concentrations have been shifting from summer to late spring and early fall. Ozone exceedances that occur in the late spring and early fall may be impacted by different VOC species than ozone exceedances that occur in the summer.

Chapter 3 – Review of the Primary Standard

What are the CASAC views on the approach described in Chapter 3 to considering the health effects evidence and the risk assessment in order to inform preliminary conclusions on the primary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current primary standard?

Air Quality

The EPA states in section 3.1.2.2 that "Analyses described in detail in the [Health Risk and Exposure Assessment] HREA suggested that reductions in O_3 precursors emissions in order to meet a standard with an 8-hour averaging time, coupled with the appropriate form and level, would be expected to reduce O_3 concentrations in terms of the metrics reported in epidemiologic studies to be associated with respiratory morbidity and mortality (80 FR 65348, October 26, 2015)." However, multiple ozone chemistry analyses (e.g., Downey et al., 2015; Simon et al., 2012) have demonstrated that peak and lowest daily ozone concentrations both decrease (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. The non-CASAC member consultants generally agreed that decreasing peak ozone concentrations will not consistently decrease the mean ozone concentrations and therefore decreasing peak ozone is not necessarily expected to improve the metrics associated with

respiratory mortality and morbidity in epidemiology studies. The CASAC recommends that the EPA reconsider their statement.

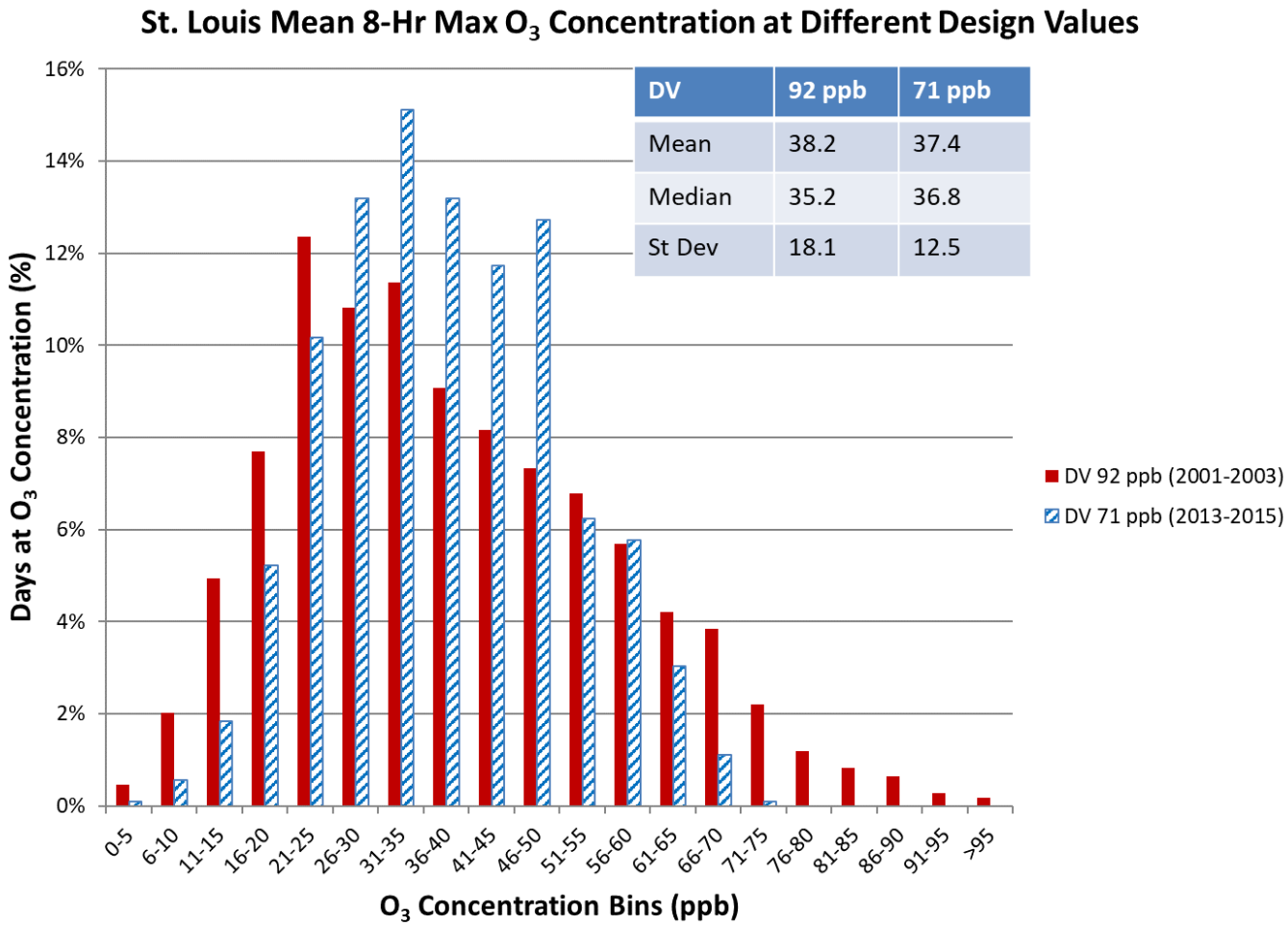

Figure 1. Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV – design value. Data from EPA's Air Quality System and analyzed similarly to the analyses in Lange (2018).

Health Effects Evidence and Risk Assessment

Accurate & Balanced Reporting

A few places in this document require some editing to ensure fully accurate and balanced reporting of data and analyses.

In several places the EPA summarizes the causality designations as: "The current evidence primarily continues to support our prior conclusions regarding the key health effects associated with O_3 exposure." (Section 3.3.1, Section 3.5.1). This should be revised: the sentences following that statement in these sections discusses that there have been some substantial changes in the causality determinations since the last review.

In Section 3.3.1.1, the EPA states that "Evidence regarding respiratory infections and associated effects has been augmented by a number of epidemiologic studies reporting positive associations between short-term O_3 concentrations and emergency department visits for a variety of respiratory infection endpoints (draft ISA, Appendix 3, Section 3.1.7.4)." Section 3.1.7.4 of the Ozone ISA also shows a number of studies that do not report positive associations between ozone and infections. Chapter 3 should provide a more balanced report of epidemiology results.

Fully Justified Conclusions

Chapter 3 requires some editing to ensure that stated conclusions are fully supported.

Section 3.3.1.2 (Other Effects) does not adequately explain why the evidence for metabolic effects is *likely causal*. The data are mostly from animal studies with high exposure levels. There is limited concordance with human epidemiology studies, and some of the evidence is contradictory. Similar limitations hold for long-term exposure and metabolic effects. The CASAC recommended in comments on the Draft Ozone ISA that the EPA reconsider the causality determination between short-term and long-term ozone exposure and metabolic effects. For the Ozone PA, the CASAC recommends that the causality determination for metabolic effects be updated to reflect the Final Ozone ISA.

Additional Policy-Relevant Information

In Section 3.3.2, it would be helpful to add a discussion of what fraction of the population (particularly at-risk populations if possible) is expected to spend 6.6 hours or more outdoors at moderate exertion. This information would aid decision makers in comparing exposure likelihood to the primary controlled human exposure (CHE) studies.

Section 3.3.2 (Public Health Implications and At-Risk Populations) lacks adequate discussion about greater susceptibility for minority and/or lower socioeconomic status (SES) populations. More information about these populations should be included.

In the risk assessment conducted for the 2015 Ozone NAAQS, the EPA included risk estimates for outdoor workers. Those risk estimates could be discussed in this document to address that potentially at-risk population.

Study Limitations

The CASAC commends the EPA for its important caveats in Section 3.3.3, stating that "We have also considered what may be indicated by the epidemiologic studies regarding exposure concentrations associated with health effects, and particularly by such concentrations that might occur in locations when the current standard is met. In so doing, however, we recognize that these studies are generally focused on investigating the existence of a relationship between O_3 occurring in ambient air and specific health outcomes, and not on detailing the specific exposure circumstances eliciting such effects…These studies generally do not measure personal exposures of the study population or track individuals in the population with a defined exposure to O_3 alone. Notwithstanding this, we have considered the epidemiologic studies identified in the draft ISA as to what they might indicate regarding O_3 exposure concentrations in this regard."

Clarity of Presentation

To ensure that data and analyses are clearly reported, Section 3.2 (General Approach and Key Issues in this Review) should clarify the purpose of the risk assessment in the policy assessment evaluation, and how it is used in the decision-making process.

In Section 3.4.2 (Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard) and elsewhere, population exposure estimates (i.e., the estimates of percent of the population exposed to certain concentrations of ozone) are referred to as risk estimates. Definitions of risk and exposure should be clarified.

The Draft Ozone PA presents quite different risk estimates produced by the McDonnell Stewart Smith model (MSS) and exposure-response (E-R) models. These are discussed at length in Appendix 3D, with an in-depth justification of the choice of the E-R model risk results over the MSS results. The EPA should add more of the information from Appendix 3D to the main text.

The EPA states that "The limited evidence that informs our understanding of potential risk to people with asthma is uncertain but indicates the potential for them to experience greater effects or have lesser reserve to protect against such effects than other population groups under similar exposure circumstances, as summarized in Section 3.3.4 above." But the potential for people with asthma to experience greater effects, and their responses caused by diminished reserve, need to be distinguished and discussed separately.

Focus on Lung Function Decrements in the Risk Analysis

The CASAC has the following concerns about the approach taken for the ozone risk assessments presented in the Draft Ozone PA. The essentially exclusive use of lung function decrements in assessing ozone risk does not adequately consider other respiratory effects that are likely to be important in people with respiratory diseases such as asthma. The following summary points are addressed below: 1) Asthma is a complex disease, with several important features beyond airflow limitation; 2) Many of the key features of asthma pathophysiology can be affected by exposure to ozone; 3) The risk assessments are based almost exclusively on studies in healthy adults and make unverified assumptions about ozone health effects in children with asthma.

1. Asthma is a complex disease (Fanta, 2009). It involves airflow limitation, airway inflammation, and nonspecific airways hyperresponsiveness. Injury to, and increased permeability of, the airway epithelium is an increasingly recognized feature of the disease. Remodeling of the airways is also part of asthma, with thickening of the submucosal basement membrane consistently seen in lung biopsies of people with asthma, even in those with normal pulmonary function.

   Many people with asthma have normal lung function and are asymptomatic at baseline, but other features of the disease, including airway inflammation and airways hyperresponsiveness, persist even when they are in remission from the symptoms of the disease. Most children with asthma are able to be active and exercise outdoors. They develop problems when something triggers an exacerbation, such as exposure to an allergen to which they are sensitized, a respiratory infection, or air pollutants, among others. Arguably the most important potential adverse effect

of acute ozone exposure in a child with asthma is not whether it causes a transient decrement in lung function, but whether it causes an asthma exacerbation.

2. Ozone has respiratory effects beyond its well-described effects on lung function. It increases airway inflammation, a key component in the pathophysiology of asthma. Eosinophilic inflammation is particularly important in allergic asthmatics, and we know from clinical studies that airway eosinophilia is increased in response to ozone exposure in asthmatics (Peden et al., 1997), especially when ozone is combined with an allergen challenge (Vagaggini et al., 2002). Ozone increases non-specific airways hyperresponsiveness in clinical studies. Ozone exposure causes airway epithelial injury and increases airway epithelial permeability, both cardinal features in asthma pathophysiology. This increases the potential for materials deposited in the distal airways, such as particles or allergens, to reach the lung interstitium and vascular space. These effects beyond lung function decrements likely contribute to the risk of an asthma exacerbation. Yet they are not captured or considered in the Draft Ozone PA's risk analysis.

   EPA's current approach minimizes the full spectrum of potential ozone airway effects. The focus in the risk assessment is solely on FEV_1, because that database is robust. But we know from other studies that the FEV_1 response and the airway inflammatory response occur via different mechanisms (Torres et al., 1997; Frampton et al., 1997; Balmes et al., 1996), and some people are more prone to one of these effects than the other. This means that there are individuals who will experience increases in airway inflammation without lung function decrements, or symptoms. The absence of symptoms could result in a failure of the individual to limit exposure, thereby further worsening the airway inflammatory effect of the exposure.

   It is reasonable to expect that, in people with asthma, any increase in airway inflammation is an adverse effect, with the potential to increase the risk for an asthma exacerbation. Repeated episodes of airway inflammation may enhance airway remodeling, which occurs in asthma, and leads to irreversible reductions in lung function.

3. The Draft Ozone PA makes the following assumptions:
   a. *Lung function decrements in response to 7-8 hour exposures near 70 ppb are the same in children with asthma as they are in healthy adults.* The clinical data in people with mild to moderate asthma, exposed at higher concentrations than those directly relevant to the standard, suggest that people with asthma do not have markedly increased FEV_1 declines compared with healthy subjects. But it is inappropriate to assume that this extends to lower concentrations, or to people with more severe disease. People with asthma do appear to experience greater effects on measures of airway obstruction, including airways resistance testing. This is briefly reviewed in the Draft Ozone ISA, but not considered in the risk assessment. None of the low-concentration, 6- to 7-hr studies listed in Tables 3A-1 and 3A-2 included people with asthma. Very few clinical studies have included severe or even moderate asthma, let alone children with asthma, and none have included people with unstable asthma or those prone to exacerbations. This is a key knowledge gap and raises legitimate questions about whether the current standard provides an adequate margin of safety for people with asthma.
   b. *Absence of symptoms means less adversity.* The Draft Ozone PA seems to suggest that lung function decrements in the absence of symptoms do not represent an adverse health effect. But this should not apply to children with asthma, for the reasons discussed above, and as

addressed more fully in the European Respiratory Society/American Thoracic Society statement on adverse health effects of air pollution (Thurston et al., 2017).

c. *Lung function and other respiratory effects are rapidly reversible in asthmatic children, similar to healthy adults*. The time course of the pulmonary function response is well-established in healthy adults, but less well in children, and especially in children with asthma. There are no data on the persistence of respiratory effects in people with asthma following low-concentration, more prolonged exposures.

The EPA should further address these points in the Draft Ozone PA, discuss how FEV_1 decrements are not the only relevant health effect from ozone exposure, and explicitly consider how these points impact the interpretation and application of the risk assessment results.

Risk Models

Chapter 3 and its supporting appendices predict risks using models and assumptions that have not been validated for predicting how changes in ozone affect public health risks. They omit important caveats similar to those provided in the EPA's 2014 Ozone HREA. These included the following for the 2012 MSS model (emphases added):

- "Clearly the **intra-individual variability**… in the MSS model is a key parameter and is influential in predicting the proportions of the population with FEV_1 decrements >10 and 15%. **The assumption that the distribution of this term is Gaussian is convenient for fitting the model, but is not accurate**. The extent to which this mis-specification affects the estimates of the parameters of the MSS model and its predictions is not clear."
- "Although **the model does not have good predictive ability for individuals** (pseudo-R2 0.28), it does better at predicting the proportion of individuals with FEV1 decrements 10, 15, and 20% (psuedo-R2s of 0.78, 0.74, 0.68) (McDonnell et al., 2012). The clinical studies that these model estimates are based on were conducted with young adult volunteers rather than randomly selected individuals, **so it may be that selection bias has influenced the model parameter estimates**. The parameter estimates are not very precise, partly as the result of correlations between the parameter estimates….The MSS model is also sensitive to the exposure concentrations, but we have not quantified that sensitivity….**We are unable to properly estimate the true sensitivities or quantitatively assess the uncertainty of the MSS model**….As discussed in Section 6.5.3 below, there are uncertainties in extrapolating the MSS model down to age 5 from the age range of 18 to 35 to which the model was fit.…[T]he uncertainty of the extension to children of the MSS model could be substantial." Section 6.5.7 adds that "EPA staff have identified key sources of uncertainty with respect to the lung function risk estimates. These are: the physiological model in APEX for ventilation rates, the O_3 exposures estimated by APEX, the MSS model applied to ages 18 to 35, and extrapolation of the MSS model to children ages 5 to 18.…**At this time we do not have quantitative estimates of uncertainty for any of these**."

The Draft Ozone PA does state that "We are using this model to estimate lung function decrements for people ages 5 and older. However, this model was developed using only data from individuals aged 18 to 35 and the age adjustment term [$\beta 1 + \beta 2\ (Age_{ijk} - 23.8)$] in the numerator of Equation 3D-13 is not appropriate for all ages." However, the fact that the model predictions are based on assumptions that are unlikely to be accurate (e.g., that the parameter alpha 2 in Table 3D-21 quadruples on one's 18th

birthday) and that the models and their predictions have not been empirically validated or verified should be emphasized. In effect, the Draft Ozone PA selects some specific parametric models and uses them to make risk predictions, but the validity of the models and their predictions is unknown. The final PA should discuss the internal and external validity of the risk models and their predictions and should present the results of empirical validation tests for the risk models and predictions.

Quantitative Uncertainty Analysis

The EPA does not provide uncertainty bounds on their exposure or risk estimates. The ranges presented represent variability between cities, not uncertainty. There are many ways that some measure of uncertainty can be accounted for in these estimates, some of which are discussed and presented in Appendix 3 – these should be included in the main text to provide information for decision making. For example, on page 3D-145, the EPA references the work of Glasgow and Smith (2017), who provide a method for quantitative uncertainty evaluation. There is also an upper bound estimate of the E-R function that is presented in Table 3D-64 – if there was an upper and lower bound function provided, then those could simply be used for some quantification of uncertainty.

The EPA discusses uncertainties with air quality analysis in Section 3.4.4 (Key Uncertainties) as well as the ways in which they have tried to reduce this uncertainty. However, this type of uncertainty is a prime candidate for a quantitative uncertainty analysis because there are estimates on the uncertainties associated with the air quality estimates.

Appendices 3C and 3D

The more detailed discussion on selection of study areas should be moved from Section 3D.2.1 to Section 3C.2 since Appendix 3C is presented prior Appendix 3D. It appears that Sacramento (2017 design value = 86 ppb) does not meet the second selection criteria listed on page 3D-14, "Combined statistical area (CSA)/metropolitan statistical area (MSA) ambient air 24 monitor design values are between 60-80 ppb, thus having minimal adjustment needed to just meet the current 8-hr O_3 NAAQS". A reason for selecting this study area should be added to the document.

It appears that the CAMx chemical transport model was only run with 2016 meteorology while the APEX exposure model was run using 2015-2017 meteorological data. The document should explain how these two models were combined to generate 2015-2017 exposures.

A comparison of 2016 emissions used in the CAMx model (Table 3C-4) to the 2014 NEI emissions (Figure 2-1) show similar emissions for CO and VOCs (after adjusting for year-specific biogenic emissions). However, the anthropogenic NOx emissions in 2016 are 20% lower than the anthropogenic NOx emissions in 2014. This large difference should be explained.

The EPA performed an ozone model performance evaluation (MPE) for each study area. However, additional explanation is needed to describe the time series plots shown on pages 3C-34 – 3C-61. It appears that the measured MDA8 is averaged for all monitors in an area and compared to the modeled MDA8 average for all monitors in the area. The document should explain how the modeled MDA8 average is calculated when observations are missing. For example, do the corresponding model results get removed or do they remain in the average? Also, it appears that the "# of sites" included in the top right corner of each plot includes both CSA and "buffer" sites. It would be more informative to evaluate

sites inside the CSA and outside the CSA (the "buffer" sites) separately. The "# of sites" shown in Figure 3C-25 for January is "14". However, Georgia only has two year-round monitors in the state. For each study area and season, it would be useful to plot all hourly observed and modeled concentrations in a single 24-hour diurnal plot with means and standard deviations (similar plot as Figure 3C-67).

The document should include the number of monitors used in each model performance summary table contained on pages 3C-31 – 3C-59. It is unclear if the "buffer" sites are included along with the CSA sites. Again, it would be more informative to evaluate sites inside the CSA and outside the CSA (the "buffer" sites) separately for each study area.

In addition to the ozone MPE, it would be useful to perform an MPE for the ozone precursors (NOx and VOCs). If the precursor concentrations don't match the observations, the HDDM sensitivity results may not be accurate even if the ozone concentrations match observations.

Figures 3C-67 and 3C-75 for Atlanta are both missing the "75 ppb" ozone distributions. Although NOx emissions were not adjusted in Atlanta for the 75 ppb scenario, the modeling results for the 75 ppb scenario should still be included.

Section 3C.5.2.2.3 should discuss why NOx reductions alone were selected for adjusting design values. In many cases, VOC reductions occur simultaneously with NOx reductions. Also, many areas of the county are equally as sensitive to VOC reductions as NOx reductions.

Section 3C.6 discusses interpolation of adjusted air quality using Voronoi Neighbor Averaging (VNA). A justification for choosing VNA over other methods should be included and its uncertainty quantified.

The exposure and risk results from the 7 study areas that are in common with the previous ozone HREA review should be compared and similarities/differences discussed in this document.

There is a figure (referenced in page 3D-91) that seems to be labeled as "0", instead of with the figure number.

Page 3D-80. For the MSS model, lung function decrements are assumed to be 0 for age >55 yrs. This model does not incorporate newer data on lung function effects in healthy older subjects (Frampton et al., 2017), which demonstrated lung function effects in subjects older than 55 yrs. This should be acknowledged in the PA.

In the Appendices, in a number of locations, there is the statement "Error Reference Not Found!" - these need to be located and fixed.

<u>Other Notes</u>

In section 3.3.1.1 Footnote: "As recognized in Section 3.3.1.1 above, the single newly available 6.6-hour study is for subjects aged 55 years of age or older, and has a slightly lower target ventilation rate for the exercise periods. The exposure concentrations were 120 ppb and 70 ppb, only the former of which elicited a statistically significant FEV1 decrement in this age group of subjects (draft ISA, Appendix 3, section 3.1.4.1.1.2)." This seems to be a typo - the Arjomandi study was a 3-hour exposure, not a 6.6-hour exposure.

In Section 3.4.1 (Conceptual Model and Assessment Approach), p. 3-50, line 7: Rather than "assessing exposure, ventilation rate, intake dose, and estimated health risk," the CASAC suggests "estimating exposure, ventilation rate, ozone intake, and health risk."

The end of the second bullet point on page 3-51 is cut-off mid-sentence.

The last sentence of the first paragraph on page 3-82 needs to be edited - there seem to be words missing or juxtaposed.

Conclusions

The CASAC agrees that the evidence newly available in this review that is relevant to setting the ozone standard does not substantially differ from that of the 2015 Ozone NAAQS review. Some of the CASAC agree with the EPA that the available evidence does not call into question the adequacy of protection provided by the current standard, and thus support retaining the current primary standard. Other members of the CASAC think that the current ozone primary standard does not provide an adequate margin of safety in the protection of children with asthma.

Chapter 4 – Review of the Secondary Standard

What are the CASAC views on the approach described in chapter 4 to considering the evidence for welfare effects in order to inform preliminary conclusions on the secondary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current secondary standard?

Background on the Current Standard

The current secondary standard for ozone was set in 2015, based on the scientific and technical information available at that time, as well as the Administrator's judgements regarding the available welfare effects evidence, the appropriate degree of public welfare protection for the revised standard, and available air quality information on seasonal cumulative exposures that may be allowed by such a standard (80 FR 65292, October 26, 2015). With the 2015 decision, the Administrator revised the level of the secondary standard for photochemical oxidants, including O_3 to 0.070 ppm (70 ppb) in conjunction with retaining the indicator (O_3), averaging time (8 hours), and form (4^{th}-highest annual daily maximum 8-hour average concentration, averaged across three years).

The welfare effects evidence base available in the previous NAAQS review included decades of extensive research on the phytotoxic effects of O_3, conducted both in and outside of the United States that documents the impacts of ozone on plants and their associated ecosystems (U.S. EPA, 1978, 1986, 1996, 2006, 2013).

In light of the extensive evidence base, the 2013 ISA concluded there was a causal relationship between ozone and visible foliar injury, reduced vegetation growth, reduced productivity in terrestrial ecosystems, reduced yield and quality of agricultural crops, and alteration of belowground biogeochemical cycles. In addition, the 2013 ISA concluded there was likely to be a causal relationship between O_3 and reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial

ecosystem water cycling, and alteration of terrestrial community composition. Further, based on the then available evidence with regard to O_3 effects on climate, the 2013 Ozone ISA also found there to be a causal relationship between changes in tropospheric ozone concentrations and radiative forcing, found there likely to be a causal relationship between tropospheric ozone concentrations and effects on climate as quantified through surface temperature response, and found the evidence to be inadequate to determine if a causal relationship exists between tropospheric ozone concentrations and health and welfare effects related to UV-B shielding.

The 2015 secondary standard for ozone was a public welfare policy judgment made by the Administrator, which drew upon the available scientific evidence for O_3-attributable welfare effects and on analyses of exposures and public welfare risks based on impacts to vegetation, ecosystems and their associated services, as well as judgements about the appropriate weight to place on the range of uncertainties inherent in the evidence and analyses.

Considerations Regarding Adequacy of the Prior Standard

The Administrator's conclusion in the previous NAAQS review regarding the adequacy of the secondary standard that was set in 2008 (0.075 ppm, as annual 4th-highest daily maximum 8 hour average concentration averaged over three consecutive years) gave primary consideration to the evidence of growth affects in well-studied tree species and information in cumulative seasonal ozone exposures in certain study areas. In doing so, the exposure information for Class I areas was evaluated in terms of the W126 Cumulative Seasonal Exposure Index, an index recognized by the 2013 Ozone ISA as a mathematical approach "for summarizing ambient air quality information in a biologically meaningful form for ozone vegetation effects purposes." The EPA focused on the W126 index for this purpose consistent with the evidence of the 2013 Ozone ISA and advice from the CASAC. The Administrator gave particular weight to analysis with focus on exposures in Class I areas, which are lands that Congress set aside for specific uses intended to provide benefits to the public welfare, including lands that are to be protected so as to conserve the scenic value and the natural vegetation and wildlife within such areas and to leave them unimpaired for the enjoyment of future generations. This emphasis on lands afforded special government protections such as national parks and forests, wildlife refuges, and wilderness areas, some of which are designated as Class I areas under the Clean Air Act, was consistent with a similar emphasis in the 2008 review of the NAAQS (73 FR 16485, March 27, 2008).

As noted across past reviews of the secondary standard for ozone, the Administrator's judgments regarding effects that are adverse to public welfare consider the intended use of the ecological receptors, resources, and ecosystems affected. Thus, in the previous NAAQS review, the Administrator utilized the median Relative Biomass Loss (RBL) estimate for the studied species as a quantitative tool within a larger framework of considerations pertaining to the public welfare significance of O_3 effects. The Administrator recognized such considerations to include effects that are associated with effects on growth and that the 2013 Ozone ISA determined to be causally or likely causally related to ozone and ambient air, yet for which there are greater uncertainties affecting estimates of impacts on public welfare. These other effects included reduced productivity in terrestrial ecosystems, reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial community composition, alteration of below ground biogeochemical cycles, and alteration of terrestrial ecosystem water cycles. The Administrator, in considering the revised lower standard, noted that a revised standard would provide increased protection for other growth-related effects, including for relative yield loss (RYL) of crops,

reduced carbon storage and for types of effects for which it is more difficult to determine public welfare significance, as well as for other welfare effects of ozone, such as visible foliar injury (80 FR 65390, October 26, 2015).

In reaching a conclusion in the amount of public welfare protection from the presence of ozone in ambient air that is appropriate to be afforded by a revised secondary standard, the Administrator gave particular consideration to the following:

1. The nature and degree of effects of O_3 on vegetation;
2. The strength and limitations of the available and relevant information;
3. Comments from the public on the Administrator's proposed decision; and
4. The CASAC reviews regarding the strength of the evidence and its adequacy to inform judgements on public welfare protection.

It was also noted that the Clean Air Act does not require that a secondary standard be protective of all effects associated with a pollutant in the ambient air, but rather those known or anticipated effects judged "adverse to the public welfare."

Does the Current Evidence Alter Conclusions from the Last Review Regarding the Nature of Welfare Effects Attributable to O_3 in Ambient Air?

The evidence newly available in this current NAAQS review supports, sharpens, and expands on the conclusions reached in the previous NAAQS review. Consistent with the evidence in the last NAAQS Review, the currently available evidence describes an array of ozone effects on vegetation and related ecosystem effects as well as the role of ozone in radiative forcing and effects on temperature, precipitation, and related climate variables. Evidence newly available in this review augments more limited previously available evidence related to insect interaction with vegetation, contributing to conclusions regarding ozone effects on plant-insect signaling and on insect herbivores. Thus, the conclusions reached by the EPA in the last NAAQS review are supported by the current evidence base and conclusions are reached in a few new areas based on the now expanded evidence. The current Draft Ozone PA details of effects of ozone on vegetation and ecosystem processes are reviewed in detail and updated with newly available evidence.

Public Welfare Implications

The public welfare implications of the evidence regarding ozone welfare effects are dependent on the type and severity of the effects, as well as the extent of the effect at a particular biological or ecological level of organization. In the Draft Ozone PA, the EPA discusses such factors in light of judgements and conclusions made in prior reviews regarding effects on the public welfare. As provided in Section 109(b)(2) of the Clean Air Act, the secondary standard is to "specify a level of air quality the attainment and maintenance of which in the judgement of the Administrator…is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air." The secondary standard is not meant to protect against all known or anticipated ozone related welfare effects, but rather those that are judged to be adverse to the public welfare in a bright line determination of adversity it is not required in judging what is requisite. Thus, the level of protection from known or anticipated adverse effects to public

welfare that is requisite for the secondary standard is a public welfare policy judgement to be made by the Administrator.

Is There Information Newly Available in this Review Relevant to Consideration of the Public Welfare Implications of Ozone Related Welfare Effects?

The categories of effects identified in the Clean Air Act to be included among welfare effects are quite diverse and, among these categories, any single category includes many different types of effects that are of broadly varying specificity and level of resolution. For instance, effects on vegetation is a category identified in the Clean Air Act Section 302(h), and the Draft Ozone ISA recognized numerous vegetation related effects of ozone at the organism, population, community, and ecosystem level. In the decisions to revise the secondary standard in the last two reviews (2008, 2015) the Administrator recognized that by providing protection based on consideration of effects in natural ecosystems in areas afforded special protection, the revised secondary standard would also "provide a level of protection for other vegetation that is used by the public and potentially affected by ozone including timber, produce grown for consumption and horticultural plants used for landscaping" (80 FR 65403, October 26, 2015). The EPA provides in the Draft Ozone PA, Figure 4-2 (Potential effects of O_3 on the public welfare), which does an excellent job at summarizing the potential effects of causal or likely to be causal impact of ozone on vegetation at the organism, population, community, and ecosystems levels.

Exposures Associated with Effects

The types of effects identified in Figure 4-2 of the Draft Ozone PA vary widely with regard to the extent and level of detail of the available information that describes the ozone exposure circumstances that may elicit them. Therefore, EPA organized a section in the Draft Ozone PA to address first, effects of ozone exposure on growth and yield effects, a category of effects for which information on exposure metrics and E-R relationships is most advanced. In addition, the EPA discusses the current information available regarding exposure metrics and relationships between exposure and the occurrence and severity of visible foliar injury.

Growth Related Effects

The longstanding body of vegetation effects evidence includes a wealth of information on aspects of ozone exposure that are important in influencing effects on plant growth and yield. A variety of factors have been investigated, including concentration, time of day, respite time, frequency of peak occurrence, plant phenology, predisposition, etc. In the last several reviews, based on the then available evidence, as well as advice from the CASAC, the EPA has focused on the use of cumulative, seasonal concentration-weighted index for considering the growth-related effects evidence and in quantitative exposure analyses for purposes of reaching conclusions on the Secondary Standard. More specifically, the EPA used the W126-based cumulative, seasonal metric. This metric, commonly called the W126 Index, is a non-threshold approach described as the sigmoidally weighted sum of all hourly ozone concentrations observed during a specified daily and seasonal time window, where each hourly ozone concentration is given a weight that increased from 0-1 within increasing concentration. The most well-studied data sets in this regard are those for 11 tree species seedlings and ten crops referenced and described by Lee and Hogsett (1996) and Hogsett et al. (1997). These datasets include: 1) for

growth effects on seedlings of a set of tree species, and 2) for quality and yield effects of a set of crops. These datasets, which include growth and yield response information across a range of multiple seasonal cumulative exposures, were used to develop robust, quantitative, E-R functions for reduced growth (RBL). In seedlings of the tree species and E-R functions for RYL for a set of common crops, the EPA's conclusions regarding exposure levels of ozone associated with vegetation related effects at the time of the last review were based primarily on these established E-R functions. The Draft Ozone ISA concludes that "the cumulative exposure indices, including the W126 Index, "are the best available approach for studying the effects of ozone exposure on the vegetation in the U.S." Accordingly, in this review, the EPA as in the last two reviews used the seasonal W126-based cumulative, concentration-weighted metric for consideration of the effects evidence in quantitative exposure analyses, particularly related to growth effects, which appears reasonable and scientifically sound. This information for the tree species, in combination with air quality analysis was a key consideration in the 2015 EPA decision on the level for the revised secondary standard (80 FR 65292, October 26, 2015).

Other Effects

With regard to climate-related effects, including radiative forcing, the newly available evidence in this review does not provide more detailed quantitative information regarding ozone concentrations at the national scale. Although ozone continues to be recognized as having a causal relationship with radiative forcing and a likely causal relationship with effects on temperature, precipitation, and related climate variables, the non-uniform distribution of ozone (spatially and temporally) makes the development of quantitative relationships between the magnitude of such effects in differing ozone concentrations in the U.S. challenging. Thus, the Draft Ozone ISA recognizes that "current limitations in climate modeling tools, variation across models, and the need for more comprehensive observational data on these effects represents sources of uncertainty in quantifying the precise magnitude of climate responses to ozone changes, particularly at regional scales. While these complexities affect the EPA's ability to consider specific ozone concentrations associated with differing magnitudes of climate-related effects, it does give the EPA the ability to estimate growth-related impacts of trees that can inform their consideration of the sequestration of carbon in terrestrial ecosystems, a process that can reduce tropospheric abundance of the pollutant (CO2) ranked first in importance as a greenhouse gas and radiative forcing agent.

What Are Important Uncertainties in the Evidence?

Among the categories of effects identified in past reviews, key uncertainties remain in the current evidence. The category of ozone welfare effects for which current understanding of quantitative relationships is strongest is reduced plant growth. As a result, this category was the focus of the Administrator's decision making in the last review, with RBL in tree seedlings playing the role of surrogate for the broader array of vegetation related effects that range from the individual plant level to ecosystem services. Limitations in the evidence base and associated uncertainties recognized in the last review remain and include a number of uncertainties that affect characterization of the magnitude of cumulative exposure conditions eliciting growth reductions in U.S. forests.

As recognized in the last review, there are uncertainties in the extent to which the 11 tree species for which there are established E-R functions encompass the range of ozone sensitive species in the

United States and also the extent to which they represent U.S. vegetation as a whole. Therefore, it should not be assumed that species of unknown sensitivity are tolerant to ozone.

The EPA recognized important uncertainties in extent to which the E-R functions for reduced growth in tree seedlings are also descriptive of such relationships during later life stages for which there is a paucity of established E-R relationships. In addition, the EPA recognizes limitations and their ability to estimate growth effects of tree lifetimes of year to year variation in ozone concentrations. For example, the studies on which the established E-R functions for 11 tree species are based vary in duration (such as 82 days in a single year to 555 days spanning more than one year). In the Draft Ozone PA, the EPA goes to great lengths in walking through uncertainties and recognizing limitations and data interpretation with a number of studies that they have considered. This is not unexpected due to the biological variability in response to a pollutant such as ozone in ecological systems.

Exposure and Air Quality Information

In general, the EPA decision making in the last review placed greatest weight on estimates of cumulative exposures to vegetation based on ambient air monitoring data for ozone and consideration of those estimates in light of E-R relationships for ozone related reduction in tree seedling growth. These analyses supported the consideration of the potential for ozone effects on tree growth and productivity as well as its associated impacts on a range of ecosystem services, including forests, ecosystem productivity, and community composition (80 FR 65292, October 26, 2015).

In revising the standard in 2015 to the current standard, the Administrator concluded that with revision of the standard level, the existing form and averaging time provided the control needed to achieve the cumulative seasonal exposure circumstances identified for the secondary standard. The focus of cumulative seasonal exposure primarily reflects the evidence of E-R relationships for plant growth. The 2015 conclusion was supported by the air quality data analyzed at that time. Analysis in the current review of the still more expanded set of air monitoring data, which includes 1,545 monitoring sites with sufficient data for variation of design values, documents similar findings as from the analysis of data from 2000-2013 described in the last review.

Monitoring sites with lower ozone concentrations as measured by the design value metric (based on the current form and averaging time of the secondary standard) also have lower cumulative seasonal exposures, as quantified by the W126 Index. As the form and averaging time of the secondary standard have not changed since 1997, the analyses performed have been able to assess the control exerted by these aspects of the standard in combinations with reductions in the level (i.e., from 80 ppb in 1997 to 75 ppb in 2008 to 70 ppb in 2015) on cumulative seasonal exposures in terms of the W126 Index.

In Figure 4-7 of the Draft Ozone PA, the evidence currently available leads the EPA to conclusions regarding exposure levels associated with effects as similar conclusions in the last review. Based largely on this evidence in combination with use of RBL as a surrogate, for vegetation related effects, the value of 17 ppm–hrs was the average W126 Index (over three years) was identified in the 2015 decision (80 FR 65393; October 26, 2015). As summarized above, the information available in the present review continues to indicate that cumulative seasonal exposure levels at virtually all sites

with air quality meeting the current standard fall below the level of 17 ppm-hrs that was identified when the current standard was established (80 FR 65393; October 26, 2015). Additionally, the average W126 Index in Class I areas that meet the current standard for the most recent three-year period is below 17 and at or below 13 ppm-hrs in 44 of those 46 Class I areas. In addition, in the current Draft Ozone PA, Table 4-2 summarizes distribution of W126 Index values in/near Class I areas. In summary, as is the case at all monitoring sites nationally, sites in or near Class I areas with design values at or below 70 ppb in the most recent three-year period have had a seasonal W126 Index (based on three year average) at or below 17 ppm-hrs. As was the case at the time the current standard was established, with the exception of four values that occurred nearly a decade ago in the southwest region, cumulative seasonal exposures in all Class I areas during periods that met the current standard were no higher than 17 ppm-hrs which reflects a protective level in the standard.

Based on established E-R functions for tree seedling growth reductions in 11 species, the tree seedling RBL for the median tree species is 5.3% for a W126 Index of 17 ppm-hrs, rising to 5.7% for 18 ppm-hrs, 6% for 19 ppm-hrs and 6.4% for 20 ppm-hrs. Below 17 ppm-hrs, median estimates include 4.9% for 16 ppm-hrs, 4.5% for 15 ppm-hrs, 4.2% for 14 ppm-hrs, and 3.8% for 13 ppm-hrs. These estimates are unchanged from what was indicated by the evidence in the last review.

The EPA has focused in the current review on the E-R relationships available in the last review for purposes of considering ozone exposure levels associated with growth-related impacts. Currently available evidence, including the newly available in the Draft Ozone ISA does not indicate the occurrence of ozone-related effects attributable to cumulative ozone exposures lower than was established at the time of the last review (.070 ppm). As in the last review, the currently available evidence continues to support a cumulative, seasonal exposure index as a biologically-relevant and appropriate metric for assessment of the evidence of exposure/risk information for vegetation, most particularly for growth related effects. This is reasonable, responsible, and reflects good use of scientific information by the EPA. The evidence continues to support important roles for cumulative exposure and for weighting higher concentrations over lower concentrations of ozone and ambient air. Thus, among the various such indices considered in the literature the cumulative, concentration-weighted W126 function continues to be best supported for purposes of relating ozone air quality to growth-related effects.

The RBL appears to be appropriately considered as a surrogate for an array of adverse welfare effects and based on consideration of ecosystem services and potential for impacts to the public as well as conceptual relationships between vegetation growth effects and ecosystem scale effects. Biomass loss is a scientifically sound surrogate of a variety of adverse effects that could be exerted to public welfare. In the previous review, the Administrator used RBL as a surrogate for consideration of the broader array of vegetation related effects of potential welfare significance that included effects of growth of individual sensitive species and extended to ecosystem level effects such as community composition in natural forests, particularly in protected public lands (80 FR 65406, October 26, 2015). The EPA believes, and the CASAC concurs, that information available in the present review does not call into question this approach, indicating there continues to be support for the use of tree seedling RBL as a proxy for the broader array of vegetation-related effects, most particularly those related to growth.

To What Extent Does the Available Information Alter Our Understanding of the Magnitude of Growth Reductions Expected to be of Public Welfare Significance?

It was recommended in the last review that a 6% RBL was "unacceptably high" and endeavored to identify a secondary standard that would limit three-year average ozone exposures somewhat below W126 Index values associated with a 6% RBL in the median species. This led to identification of a seasonal W126 Index value of 17 ppm-hrs that the Administrator concluded was appropriate as a target at or below which the new standard would generally restrict cumulative seasonal exposures (80 FR 65407, October 26, 2015). The currently available evidence continues to indicate conceptual relationships between reduced growth and the broader array of vegetation-related effects of ambient ozone exposure.

What Does the Information Available in the Current Review Indicate with Regards to Support for Use of a Three Year Average Seasonal W126 Index as the Cumulative Exposure Metric (Associated with a Value of 17 ppm-hrs) for Describing the Requisite Level of Protection for the Secondary Standard?

In the setting of the current standard, the EPA focused on control of seasonal cumulative exposures in terms of a three year average W126 Index metric. The evaluations in the PA for the last review recognized there to be limited information to discern differences in the level of protection afforded for cumulative growth-related effects by a standard focused on a single-year W126 as compared to a three-year W126 Index (80 FR 65390, October 26, 2015). Accordingly, the identification of the three year average for considering the seasonal W126 Index recognized that there was year-to-year variability, not just in ozone concentrations, but also in environmental factors, including rainfall and meteorological factors, that influences the occurrence and magnitude of ozone related effects in any year and contribute uncertainties to interpretation of the potential for harm to public welfare over the longer term. Based on this recognition, as well as other considerations, the Administrator expressed greater confidence in judgements related to public welfare impacts based on seasonal W126 Index estimated by a three-year average and accordingly relied on that metric, which appears of reasonable thought and scientifically sound.

Does the Currently Available Scientific Evidence in Air Quality and Exposure Analyses Support or Call into Question the Adequacy of the Protection Afforded by the Current Secondary Ozone Standard?

As delineated by the Clean Air Act, the secondary standard is meant to protect against ozone-related welfare effects that are judged to be adverse to the public welfare. The EPA, in development of the Draft Ozone PA, considered the currently available information regarding welfare effects of ozone in this context, while recognizing that the level of protection from known or anticipated adverse effects to public welfare that is requisite for the secondary standard, is a public welfare policy judgement made by the Administrator. The EPA considered the quantitative analyses, including associated limitations and uncertainties and the extent to which they indicate differing conclusions regarding the level of protection indicated to be provided by the current standard from adverse effects. The EPA additionally considered the key aspects of the evidence in air quality/exposure information emphasized in establishing the current standard and the associated public welfare policy judgements and judgements about inherent uncertainties that are integral to decisions on the adequacy of the current secondary standard for ozone. In considering the currently available evidence, the EPA

recognized the long-standing evidence base of the vegetation-related effects of ozone, augmented in some aspects since the last review. Consistent with the evidence in the last review, the currently available evidence describes an array of ozone effects on vegetation and related ecosystem effects as well as the role of ozone in radiative forcing with effects on climate related variables. The current evidence base supports conclusions of causal relationships between, particularly, vegetation and other endpoints and likely to be causal relationships between other endpoints that the EPA thoroughly discussed in the Draft Ozone ISA. The EPA appropriately recognized uncertainties in categories of effects newly identified that could limit consideration of the protection that might be provided by the current standard against these effects.

As was the case in the last review, a category of effects for which the evidence supports quantitative description of relationships between air quality conditions and response is plant growth or yield. The evidence base continues to indicate growth-related effects as sensitive welfare effects, with the potential for ecosystem scale ramifications. For this category of effects, there are established E-R functions that relate cumulative seasonal exposure of varying magnitudes to various incremental reductions in expected tree seedling growth (in terms of RBL) and in expected crop yield. Decades of research also recognizes visible foliar injury as an effect of ozone, although uncertainties continue to hamper efforts to quantitatively characterize the relationship of its occurrence and relative severity with ozone exposures.

Reviews of NAAQS also required judgements on the extent to which particular welfare effects (such as with regard to type, magnitude/severity, or extend) are important from a public welfare perspective. In the case of ozone, such a judgement includes consideration of the public welfare significance of small estimates of RBL and associated unquantified potential for larger scale effects. With regard to public welfare significance of 5-6% RBL, the EPA notes CASAC characterization of 6% RBL (in seedlings of median tree species) in the last review. The rationale provided by the CASAC with this characterization was primarily conceptual and qualitative rather than quantitative. The conceptual characterization recognized linkages between effects on the plant level scale and broader ecosystem impacts, and this facilitated the Administrator consider RBL as a surrogate for the broader impacts that could be elicited by ozone. In the 2015 decision, the Administrator took note of CASAC advice regarding use of RBL as a proxy and set the standard with "underlying objective of a revised Secondary Standard that would limit cumulative exposures in nearly all instances to those for which the median RBL estimate would be somewhat lower than 6%" (80 FR 65407, October 26, 2015). The 2015 decision noted that "the Administrator does not judge RBL estimates associated with marginal higher exposures [at or above 19 ppm-hrs] in isolated rare instances to be indicative of adverse effects to the public welfare" (80 FR 65407, October 26, 2015).

In considering the quantitative analyses available in the Draft Ozone PA, the EPA noted the findings from the analysis of recent air quality at sites across the United States, including in or near 64 Class I areas and also analysis of historical air quality. Findings from the analysis of air quality data from the most recent period and from the larger analysis of historical air quality data extended back to 2000 are consistent with the air quality analysis findings that were part of the basis for the current Standard. That is, in virtually all design value periods and in all locations at which the current Standard was met, the three-year average W126 metric was at or below 17 ppm-hrs, the target identified by the Administrator in establishing the current standard (80 FR 65404-65410, October 26, 2015).

The EPA summarized in the Draft Ozone PA that there is little in the information available in the current review that differs from that in the last review that relate to key aspects of the judgments and associated decision that established the current standard in 2015. The new information available is consistent with that available in the last review for the principle effects for which the evidence is strongest (such as growth, reproduction, and related larger scale effects, as well as visible foliar injury).

General Comments

1. The CASAC compliments the EPA on a very thorough and well-written Chapter 4.
2. The foundation upon which scientific data were utilized while also incorporating concepts of judgement on behalf of the EPA with input from various entities lays a strong and clear scientific process of considerations for the preliminary conclusions on the current secondary standard.
3. The preliminary conclusion by the EPA that the 2015 decision to revise the level of the secondary standard for photochemical oxidants, including ozone to .07 ppm (70 ppb) in conjunction with retaining the indicator (O_3), averaging time (8 hours) and form (4^{th} highest annual daily maximum 8-hour average concentration, averaged across three years) appears to be working in maintaining ambient air concentrations of ozone across the United States at levels that are protective for the public welfare, particularly as related to vegetation.
4. RBL appears to be appropriately considered as a surrogate for an array of adverse welfare effects and based on consideration of ecosystem services and potential for impact to the public as well as conceptual relationships between vegetation growth effects and ecosystem scale effects. The CASAC agrees that biomass loss, as reported in RBL, is a scientifically-sound surrogate of a variety of adverse effects that could be exerted to public welfare.
5. The EPA believes, and the CASAC concurs, that information available in the present review does not call in to question this RBL approach, indicating that there continues to be support for the use of tree seedling RBL as a proxy for the broader array of vegetation related effects, most particularly those related to growth that could be impacted by ozone.
6. It was recommended in the last review that a 6% RBL was "unacceptably high" and endeavored to identify a secondary standard that would limit three-year average ozone exposure somewhat below W126 Index values associated with a 6% RBL in the median species, and the CASAC concurs that this strategy is still scientifically reasonable. The identification of a seasonal W126 Index value of 17 ppm-hrs that the EPA concludes appropriate as a target at or below which the Secondary Standard would generally restrict cumulative seasonal exposure. The CASAC believes that this target is still effective in particularly protecting the public welfare in light of vegetation impacts from ozone.
7. On August 23, 2019, the D.C. Circuit Court issued an opinion concluding, in relevant part, that the EPA had not provided a sufficient rationale for aspects of its decision on the 2015 secondary standard (Murray Energy v. EPA, 936 F.3d 597 [D.C. Cir. 2019]). Accordingly, the court remanded the secondary standard to the EPA for further justification or reconsideration, particularly in relation to its decision to focus on a 3-year average for consideration of the cumulative exposure, in terms of W126, identified as providing requisite public welfare protection, and its decision to not identify a specific level of air quality related to visible foliar injury. It is not clear if the EPA has fully addressed this concern in the Draft Ozone PA.
8. Figure 4D-3 containing a scatter plot of W126 versus 8-hour ozone design values based on 2015-2017 data should be included in Chapter 4 to justify the use of the 8-hour ozone design as a surrogate for W126.

9. The CASAC recommends that the Draft Ozone PA should more thoroughly address effects of ozone on climate change by providing quantitative estimates and uncertainty bands for effects of ozone on global warming and the consequence for economic and welfare effects on the United States. At a minimum, estimates of the change in warming caused by a change in ozone should be discussed and implications for human welfare in the United States should be evaluated.
10. The approach described in Chapter 4 to considering the evidence for welfare effects is laid out very clearly, thoroughly discussed and documented, and provided a solid scientific underpinning for the EPA conclusion leaving the current secondary standard in place.

Future Research

What are the CASAC views regarding the areas for additional research identified in Chapters 3 and 4? Are there additional areas that should be highlighted?

The CASAC recommends that the following be included as important areas of future research:

- PAMS monitoring information for the months of April through October in ozone nonattainment areas, since peak ozone concentrations have been shifting from summer to late spring and early fall. Ozone exceedances that occur in the late spring and early fall may be impacted by different VOC species than ozone exceedances that occur in the summer.
- Further research into current ozone chemistry and how it may be impacted by climate change.
- Research into development of more efficient and effective control strategies for ozone reduction.
- Assessment of respiratory effects other than FEV_1 at ozone levels that are in the range of the current standard, particularly endpoints such as airway hyper-responsiveness and airway inflammation that are important for children with asthma.
- External validation of the FEV_1 E-R and MSS models, and validation with other FEV_1 models.
- Further research into the metabolic effects of ozone, particularly in human populations for clinical health outcomes such as metabolic syndrome, diabetes, etc., as well as intermediate indicators like insulin resistance; and in animal toxicology studies at concentrations closer to ambient concentrations.
- 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.)
- Further research into new technology to inform exposures of the general population, including at-risk/sensitive populations, to ozone.

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Appendix A

Individual Comments by CASAC Members on the EPA's
Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards
(External Review Draft – October 2019)

Dr. James Boylan

Chapter 1 – Introduction

To what extent does the CASAC find that the information in Chapter 1 is clearly presented and that it provides useful context for the review?

EPA has provided CASAC with a pool of consultants that can respond to written questions from the CASAC. Although the pool of consultants has provided additional insight and useful information, they do not serve the same role as a formal ozone review panel since there are no deliberations and only written answers to specific questions. I feel that the traditional review process (with pollutant specific review panels) is significantly more informative to CASAC's recommendations since it allows verbal discussions and deliberations among experts with differing backgrounds and opinions resulting in a more comprehensive examination of controversial topics.

The purpose of the PA is to bridge the gap between EPA's scientific assessments and the judgement required by the EPA Administrator when determining whether to retain or revise the NAAQS. It is unusual to review a draft PA and draft ISA simultaneously since the ISA is the scientific basis for the PA. Also, it is unusual to include the REA as part of the PA rather than a stand-alone document that is reviewed prior to the release of the draft PA. I feel that a second draft of the PA (with an updated REA) should be reviewed by the CASAC after the final ISA is released.

Chapter 2 – Air Quality

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

O_3 and Photochemical Oxidants in the Atmosphere (Section 2.1)
This section should discuss how the precursor emissions listed in this section (NOx, VOCs, CO, and CH_4) are important for ozone formation. An overview of the chemical mechanism should be presented, and important chemical reactions should be highlighted. The relative importance of each precursor should be discussed with respect to urban ozone formation vs. ozone formation in the remote troposphere. Also, the relative importance of NOx vs. VOCs should be discussed with respect to geographic location in the U.S. (e.g., SE, NE, Central, Midwest, West).

Sources and Emissions of O_3 Precursors (Section 2.2)
This section presents estimated national values for 2014 NEI emissions. However, there is no detailed discussion on the uncertainty associated with each pollutant or source sector. Some pollutants and sectors will be much more uncertain than others. For example, NOx emissions from electric generating units (EGUs) have low uncertainty since they are typically captured by hourly CEMs. On the other hand, other source sectors and pollutants may be highly uncertain. The uncertainties in the emissions inventory (magnitude, spatial allocation, and temporal allocation) should be discussed for each pollutant and source sector. In addition, it would be helpful to add national maps containing county-level emissions for NOx, VOCs, CO, and CH_4 to show the variability across the country.

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.

Ozone in Ambient Air (Section 2.4)
This section should include a discussion on ozone precursor trends in addition to ozone trends. Specifically, trends in NOx, VOCs, and CO measurements from national monitoring networks (AQS, near-road, NCore, and PAMS) should be included and discussed.

It is stated on page 2-19, "B shows the seasonal pattern for an urban site in Baton Rouge, LA. Throughout the southeastern U.S., the highest O_3 concentrations are often observed in April and May due to the onset of warm temperatures combined with abundant emissions of biogenic VOCs at the start of the growing season. This is often followed by lower concentrations during the summer months, which is associated with high humidity levels that tend to suppress O_3 formation." While this statement might be true for Baton Rouge, it does not apply to the entire southeastern U.S. In addition, a reference should be provided to support the statement that high humidity levels suppress O_3 formation.

EPA's 2016 Exceptional Events Rule allows certain ozone measurements due to natural events to be excluded from the official design values when compared to the NAAQS. In some cases, identical exceptional events can be treated differently in one location vs. another based on how close the area is to the standard. In both locations, people are impacted by adverse health effects, but the data is removed in one location and not the other. The PA should discuss how exceptional events are accounted for in the policy assessment.

Background O_3 (Section 2.5)
EPA used the CMAQ chemical transport model with the zero-out approach to estimate U.S. background, international, and natural contributions. Figures 2-22, 2-23, and 2-24 should add a 100% line. EPA should add explanations for values over the 100% line. The caption in Figure 2-26 is incorrect. The figures and tables containing USB contribution on the average of the top 10 predicted O_3 days and the 4^{th} highest O_3 days are very useful and relevant to policy decisions. These values should be compared to previous work by Jaffe (2018) and Parrish (2017, 2019). In Appendix 2B, the scale used in Figure 2B-15 should be reduced from 100% to a lower value to allow the reader to see the differences between monitoring sites.

Chapter 3 – Review of the Primary Standard

What are the CASAC views on the approach described in chapter 3 to considering the health effects evidence and the risk assessment in order to inform preliminary conclusions on the primary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current primary standard?

The more detailed discussion on selection of study areas should be moved from Section 3D.2.1 to Section 3C.2 since Appendix 3C is presented prior Appendix 3D. Sacramento (2017 design value = 86 ppb) does not meet the second selection criteria listed on page 3D-14, "Combined statistical area (CSA)/metropolitan statistical area (MSA) ambient air 24 monitor design values are between 60-80 ppb,

thus having minimal adjustment needed to just meet the current 8-hr O3 NAAQS". A reason for selecting this study area should be added to the document.

The CAMx chemical transport model was only run with 2016 meteorology while the APEX exposure model was run using 2015-2017 meteorological data. This Chapter should give a high-level explanation of how these two models were combined to generate 2015-2017 exposures with a reference to the Appendix for additional details.

A comparison of 2016 emissions used in the CAMx model (Table 3C-4) to the 2014 NEI emissions (Figure 2-1) show similar emissions for CO and VOCs (after adjusting for year specific biogenic emissions). However, the anthropogenic NOx emissions in 2016 are 20% lower than the anthropogenic NOx emissions in 2014. This large difference should be explained.

EPA performed an ozone model performance evaluation (MPE) for each study area. However, additional explanation is needed to describe the time series plots shown in pages 3C-34 – 3C-61. It appears that the measured maximum daily 8-hour average ozone (MDA8) is averaged for all monitors in an area and compared to the modeled MDA8 average for all monitors in the study area. The document should explain how the modeled MDA8 average is calculated when observations are missing. For example, do the corresponding model results get removed or do they remain in the average? Also, it appears that the "# of sites" included in the top right corner of each plot includes both CSA and "buffer" sites. It would be more informative to evaluate sites inside the CSA and outside the CSA (the "buffer" sites) separately. In fact, it would be most informative to develop individual time series plots for each monitoring site included in each study area. The "# of sites" shown in Figure 3C-25 for Atlanta in January is "14". However, Georgia only has two year-round monitors in the state. For each study area and season, it would be useful to plot all hourly observed and modeled concentrations in a single 24-hour diurnal plot with means and standard deviations (similar plot as Figure 3C-67).

The document should include the number of monitors used in each model performance summary table contained on pages 3C-31 – 3C-59. It is unclear if the "buffer" sites are included along with the CSA sites. Again, it would be more informative to evaluate sites inside the CSA and outside the CSA (the "buffer" sites) separately for each study area.

In addition to the ozone MPE, it would useful to perform a model performance evaluation for the ozone precursors (NOx and VOCs). If the precursor concentrations don't match the observations, the HDDM sensitivity results may not be accurate even if the ozone concentrations match observations.

Figures 3C-67 and 3C-75 for Atlanta are both missing the "75 ppb" ozone distributions. Although NOx emissions were not adjusted in Atlanta for the 75 ppb scenario, the modeling results for the 75 ppb scenario should still be included.

Section 3C.5.2.2.3 should discuss why NOx reductions alone were selected for adjusting design values. In many cases, VOC reductions occur simultaneously with NOx reductions. Also, many areas of the county are equally as sensitive to VOC reductions as NOx reductions.

Table 3C-19 containing percent emissions changes used for each urban area to just meet each of the 22 air quality scenarios evaluated should include a negative (-) sign for emission reductions.

It is stated on page 3-35 that "In 2016, nearly 50% of jobs held by civilian workers required outdoor work at some point during the workday." On page 3-56, it is stated "The exception to this is for outdoor workers, who due to the requirements of their job spend more time outdoors. As information for this group, including specific durations of time spent outdoors and activity data, is limited, the group was not simulated in this assessment, although we note that a targeted analysis was performed in the 2014 HREA." The footnote on page 3-57 states "Outdoor workers are not a population that has been explicitly simulated in the current analyses, and the updates to exposure duration and target ventilation rate in the current simulations would be expected to produce different results than those estimated for the 2014 REA." The PA should explain why outdoor workers were not simulated in the current analyses and if this would have a significant impact on the risk assessment.

Section 3C.6 discusses interpolation of adjusted air quality using Voronoi Neighbor Averaging (VNA). A justification for choosing VNA over other methods should be included and its uncertainty quantified.

The exposure and risk results from the 7 study areas that are in common with the 2014 ozone HREA review should be compared and similarities/differences discussed in this document.

The current form of the standard is discussed in Section 3.1.2.3. 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., 100, 98, 95 ppb) and the fourth-high value is 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 remainder of the higher end of the daily maximum 8-hour ozone average concentration distribution is ignored (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 vs. fourth-highest value) 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.

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 EPD 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 annual values (2013-2018) and 3-year design values (2015-2018). 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 is appropriate to represent the upper part of the ozone concentration distribution in Georgia. 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.

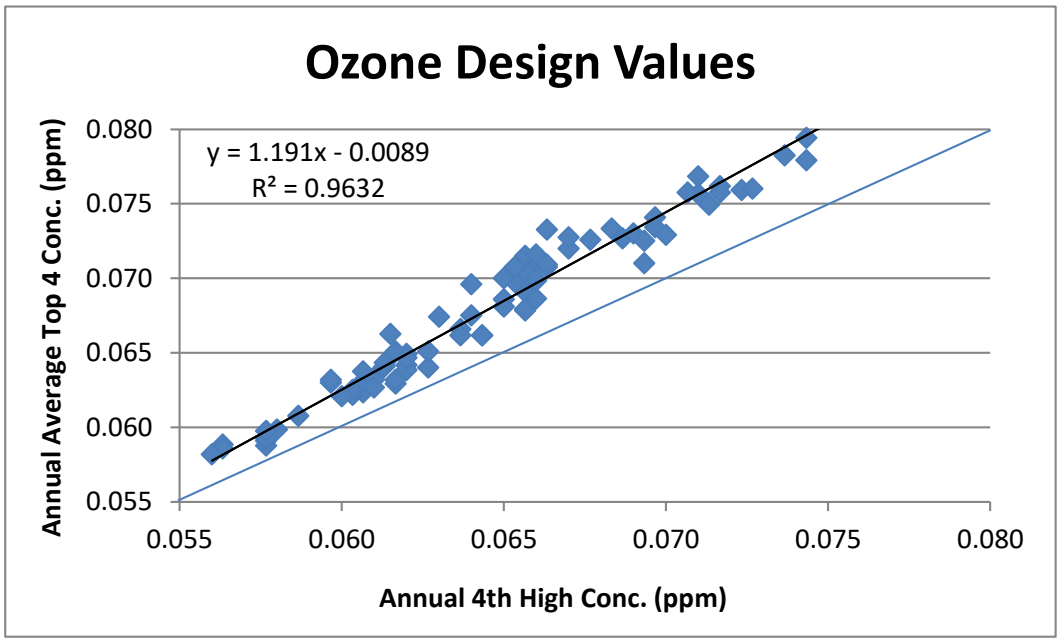

Figure 1. Comparison of the 3-year ozone design values (2015-2018) using the annual 4th high daily maximum 8-hour ozone average concentration vs. the annual average of the top 4 daily maximum 8-hour ozone average concentrations.

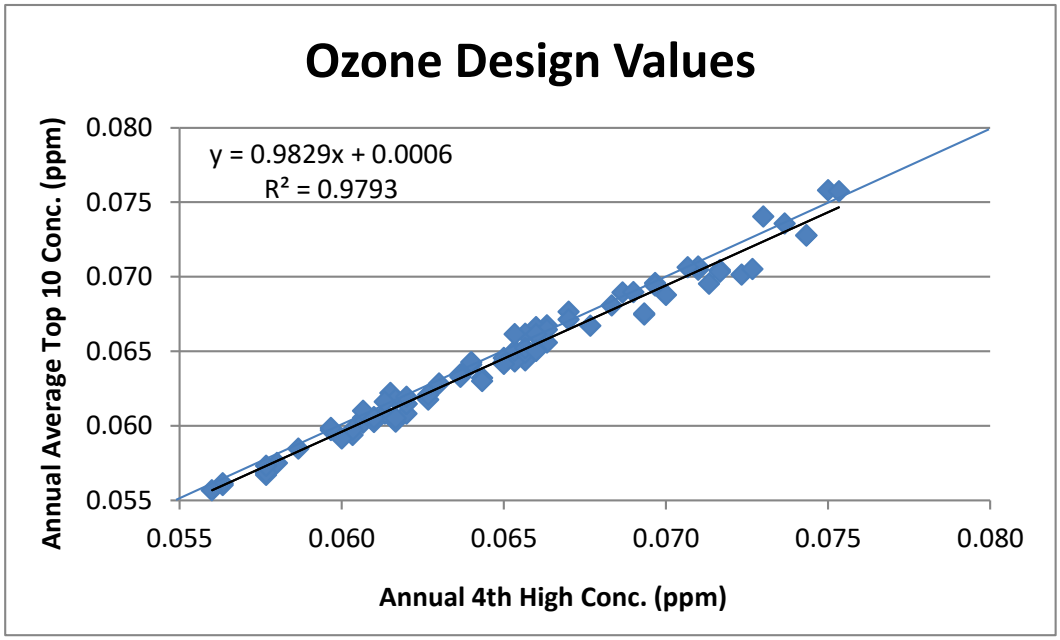

Figure 2. Comparison of the 3-year ozone design values (2015-2018) using the annual 4th high daily maximum 8-hour ozone average concentration vs. the annual average of the top 10 daily maximum 8-hour ozone average concentrations.

Chapter 4 – Review of the Secondary Standard

What are the CASAC views on the approach described in chapter 4 to considering the evidence for welfare effects in order to inform preliminary conclusions on the secondary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current secondary standard?

On August 23, 2019, the D.C. Circuit Court issued an opinion concluding, in relevant part, that EPA had not provided a sufficient rationale for aspects of its decision on the 2015 secondary standard (Murray Energy v. EPA, 936 F.3d 597 [D.C. Cir. 2019]). Accordingly, the court remanded the secondary standard to EPA for further justification or reconsideration, particularly in relation to its decision to focus on a 3-year average for consideration of the cumulative exposure, in terms of W126, identified as providing requisite public welfare protection, and its decision to not identify a specific level of air quality related to visible foliar injury. It is not clear if EPA has fully addressed this concern in this document.

Figure 4D-3 containing a scatter plot of W126 versus 8-hour ozone design values based on 2015-2017 data should be included in Chapter 4 to justify the use of the 8-hour ozone design as a surrogate for W126.

Chapters 3 and 4

What are the CASAC views regarding the areas for additional research identified in Chapters 3 and 4? Are there additional areas that should be highlighted?

EPA should consider extending the PAMS monitoring season from 3 months (June, July, August) to 6 months (mid-April, May, June, July, August, September, mid-October) in ozone nonattainment areas since peak ozone concentrations have been shifting from summer to late spring and early fall. Ozone exceedances that occur in the late spring and early fall may be impacted by different VOC species than ozone exceedances that occur in the summer.

References

Jaffe D. A., et al. (2018) Scientific assessment of background ozone over the U.S.: Implications for air quality management. Elem. Sci. Anth., 6 56 doi.org/10.1525/elementa.309.

Parrish, D. D., Young, L. M., Newman, M. H., Aikin, K. C., and Ryerson, T. B. (2017) Ozone Design Values in Southern California's Air Basins: Temporal Evolution and U.S. Background Contribution, J. Geophys. Res.-Atmos., 122, 11166–11182, https://doi.org/10.1002/2016JD026329.

Parrish, D. D. and C. A. Ennis (2019). Estimating background contributions and US anthropogenic enhancements to maximum ozone concentrations in the northern US, Atmos. Chem. Phys., 19, 12587–12605, https://doi.org/10.5194/acp-19-12587-2019.

Dr. Tony Cox

Chapter 1 – Introduction

To what extent does the CASAC find that the information in Chapter 1 is clearly presented and that it provides useful context for the review?

The discussions of legislative background and history are clearly, although briefly, presented. They provide useful context for the review.

For the final PA, it might be useful to add a discussion of the exceptional nature of the current CASAC and NAAQS review process. Specifically, relevant background on changes in processes and procedures could include: (a) further details of Administrator Pruitt's "Back to Basics" memorandum (adding to the discussion on p. 1-12); (b) the disbanding of the CASAC Particulate Matter (PM) Review Panel and streamlining of the review process to promote timely advice; (c) the appointment of a pool of non-member consultants to expand the expertise and fields of knowledge used to inform the CASAC's review; and (d) the Administrator's and CASAC's explicit emphasis on sound science throughout the review process, including reexamination of long-standing assumptions and frameworks used in previous reviews.

Relevant background on methodological changes in the current CASAC's scientific and technical approach in this review cycle could be provided in a separate section. These include the following:

(1) Drawing and preserving key conceptual distinctions between
    a. Association vs. causation
        i. Formal quantitative causal inference vs. judgment for drawing causal conclusions from data;
        ii. Manipulative or interventional causation vs. Bradford Hill or weight-of-evidence (WoE) causation;
        iii. Statistical vs. biological (mechanistic) concepts of causation;
    b. Empirically verified evidence vs. unverified assumptions and models;
    c. Estimated vs. actual individual exposures; and
    d. Explicitly derived and independently verifiable scientific conclusions vs. expert judgments.

(2) Emphasis on more effective integration of information from animal toxicology and controlled human exposure studies to:
    a. Elucidate and validate potential (i.e., hypothesized) causal biophysical mechanisms underlying epidemiologically suggested health risks; and
    b. Better characterize dose-dependent thresholds and causal biological C-R functions for pulmonary inflammation and other physiological responses in other tissues, organs, and systems in response to inhaled ozone.

The stated intentions for the Draft PA presented in Chapter 1 include "to serve as a source of policy-relevant information;" "to be understandable to a broad audience;" and "to facilitate advice to the Agency and recommendations to the Administrator" from the CASAC. The CASAC recommends that these intentions be more fully realized in the PA by undertaking the following measures:

1. *Summarize available empirical evidence on how changes in public health effects depend on changes in ozone levels.* Ideally, this information should be discussed in detail in the final ISA.
2. *Summarize results from a systematic review and critical evaluation and synthesis of relevant studies relied on to reach conclusions,* including negative studies and studies of nonlinear C-R functions for ozone that were omitted in the draft ISA but that should inform the PA.
3. Throughout the PA, *clearly distinguish between causal C-R functions (describing how public health risks change in response to changes in ambient ozone levels) and regression C-R functions* (describing how observed public health risks differ across different observed or estimated ambient ozone levels). These are in general different concepts and different curves. Causal C-R functions are relevant for policy analysis. The draft PA addresses regression C-R functions. The final PA should use validated causal C-R functions to predict effects of alternative policy choices.
4. *Increase transparency and logical soundness in deriving conclusions* by documenting exactly how conclusions were reached and validated, in enough detail so that others can trace and check the logic used. This documentation should provide clear operational definitions of the key quantities and terms used to calculate, validate, and communicate scientific results. Conclusions should address the extent to which changing NAAQS standards for ozone demonstrably causes changes in public health outcomes. Uncertainties and variability in the answers should be quantified.
5. *Distinguish between estimated and actual exposures* throughout the PA.
6. *Discuss in more detail causal biological mechanisms of inflammation-related health effects* preventable by reducing current ozone levels (including, if relevant, roles of the NLRP3 inflammasome in mediating persistent adverse health effects).
7. *Critically discuss the biological realism* of the PA's risk predictions and modeling assumptions, specifically for how public health risks are predicted to change in response to changes in ambient ozone levels.
8. *Present results of empirical validation tests* of the PA's risk predictions and modeling assumptions against observations, specifically for how public health risks have changed in response to changes in ambient ozone levels.
9. *Quantify uncertainty and variability in risk predictions, taking into account epistemic uncertainties (e.g., from model uncertainty and exposure estimation error) as well as sampling variability. Present comprehensive, quantitative uncertainty, sensitivity, and variability analyses* showing how the ISA's conclusions change for variations in selection and weighting of studies, compositions of populations (representing causally relevant interindividual variability and heterogeneity in causal C-R functions), modeling choices and assumptions, interpretations of undefined and vague terms, and subjective judgments on which the conclusions depend. These

comprehensive analyses should complement the limited set of uncertainty and variability analyses in Section 3D of the draft PA.

Chapter 3 – Review of the Primary Standard

What are the CASAC views on the approach described in chapter 3 to considering the health effects evidence and the risk assessment in order to inform preliminary conclusions on the primary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current primary standard?

Chapter 3 and its supporting appendixes predict risks using models and assumptions that have not been validated for predicting how changes in ozone affect public health risks. It omits important caveats such as those provided in the 2014 REA (www3.epa.gov/ttn/naaqs/standards/ozone/data/20140829healthrea.pdf). These included the following for the 2012 MSS model (emphases added):

- "Clearly the **intra-individual variability**… in the MSS model is a key parameter and is influential in predicting the proportions of the population with FEV1 decrements > 10 and 15%. **The assumption that the distribution of this term is Gaussian is convenient for fitting the model, but is not accurate**. The extent to which this mis-specification affects the estimates of the parameters of the MSS model and its predictions is not clear."
- "Although **the model does not have good predictive ability** for individuals (psuedo-R2 0.28), it does better at predicting the proportion of individuals with FEV1 decrements. 10, 15, and 20% (psuedo-R2s of 0.78, 0.74, 0.68) (McDonnell et al., 2012). The clinical studies that these model estimates are based on were conducted with young adult volunteers rather than randomly selected individuals, so **it may be that selection bias has influenced the model parameter estimates**. The parameter estimates are not very precise, partly as the result of correlations between the parameter estimates… The MSS model is also sensitive to the exposure concentrations, but we have not quantified that sensitivity. … **We are unable to properly estimate the true sensitivities or quantitatively assess the uncertainty of the MSS model**. … As discussed in Section 6.5.3 below, there are uncertainties in extrapolating the MSS model down to age 5 from the age range of 18 to 35 to which the model was fit. …[T]he uncertainty of the extension to children of the MSS model could be substantial." Section 6.5.7 adds that "EPA staff have identified key sources of uncertainty with respect to the lung function risk estimates. These are: the physiological model in APEX for ventilation rates, the O3 exposures estimated by APEX, the MSS model applied to ages 18 to 35, and extrapolation of the MSS model to children ages 5 to 18. … At this time **we do not have quantitative estimates of uncertainty for any of these**."

The Draft PA does state that "We are using this model to estimate lung function decrements for people ages 5 and older. However, this model was developed using only data from individuals aged 18 to 35 and the age adjustment term [$\beta 1 + \beta 2$ (Ageijk – 23.8)] in the numerator of Equation 3D-13 is not appropriate for all ages." However, the fact that the model predictions are based on assumptions that are unlikely to be accurate (e.g., that the parameter alpha 2 in Table 3D-21 quadruples on one's 18th birthday) and that the models and their predictions have not been empirically validated or verified

should be emphasized. In effect, the PA selects some specific parametric models and uses them to make risk predictions, but the validity of the models and their predictions is unknown.

The final PA should discuss empirical validation of model predictions for changes in public health risks caused by changes in ambient ozone levels across a variety of settings. It should explicitly address the extent to which the property of invariant causal prediction has been validated for the models used to make predictions of the effects of potential future changes in policies. It should comment on the internal and external validity of the risk models and their predictions, and should present the results of empirical validation tests for the risk models and predictions. Chapter 3 and its appendices should clearly distinguish between *causal* C-R functions (describing how public health risks change in response to changes in ambient ozone levels) and *regression* C-R functions (describing how observed public health risks differ across different observed or estimated ambient ozone levels). These are in general different concepts and different curves. Causal C-R functions are relevant for policy analysis. The draft PA addresses regression C-R functions. The final PA should use validated causal C-R functions (satisfying the property of invariant causal prediction if possible) to predict effects of alternative policy choices.

Dr. Mark Frampton

General Comments

The EPA time-frame and process are inadequate for CASAC to provide a considered and insightful review of this PA. The review of the ISA and the PA are being done simultaneously, when logically the PA depends on the findings of the ISA. CASAC should be provided the opportunity to review, comment on, and receive responses from EPA on the ISA, before any consideration of the PA. The EPA should use CASAC's advice on the ISA to help inform the preparation of the PA. By preparing the PA prior to CASAC's review of the ISA, EPA is short-circuiting the process, and in effect severely limiting CASAC's ability to advise EPA on the ozone NAAQS.

The failure of EPA to appoint an expert review panel to assist CASAC in its reviews of the ISA and PA, as has been done for previous CASAC reviews, has adversely affected the ability of the Committee to provide the best advice to the Administrator. Previously the expert panel has interacted directly with CASAC during the public meetings in an iterative fashion to help inform CASAC's conclusions, and that is absent with the new structure. For this ozone review, additional expertise is needed in epidemiology, toxicology, and human clinical studies, and that expertise should include active investigators in the field. While the chartered CASAC does include one physician, the review would have benefitted, especially with regard to some of the key issues in the PA, from input from additional physicians with expertise in the respiratory effects of ozone exposure and impacts on asthma. CASAC strongly recommends that future CASAC reviews are assisted by expert panels with appropriately diverse expertise that are asked to provide written reviews and be present to interact during CASAC deliberations.

Chapter 3: REVIEW OF THE PRIMARY STANDARD

There are concerns in the approach taken for the ozone risk assessments presented in this PA. The essentially exclusive use of lung function decrements in assessing ozone risk does not adequately consider other respiratory effects that are likely to be important in people with respiratory diseases such as asthma. The analyses do not adequately consider the risks for people with asthma.

The following summary points will be addressed below.

1. Asthma is a complex disease, with several important features beyond airflow limitation.

2. Many of the key features of asthma pathophysiology can be affected by exposure to ozone.

3. The risk assessments are based almost exclusively on studies in healthy adults, and make unverified assumptions about ozone health effects in children with asthma.

4. The current ozone NAAQS level of 70 ppb does not provide an adequate margin of safety for children with asthma.

1. Asthma is a complex disease [1]. It involves airflow limitation, airway inflammation, and nonspecific airways hyperresponsiveness. Injury to, and increased permeability of, the airway epithelium is an increasingly recognized feature of the disease. Remodeling of the airways is also part of asthma, with thickening of the submucosal basement membrane consistently seen in lung biopsies of people with asthma, even in those with normal pulmonary function.

Many people with asthma have normal lung function and are asymptomatic at baseline, but other features of the disease, including airway inflammation and airways hyperresponsiveness, persist even when they are in remission from the symptoms of the disease. Most children with asthma are able to be active and exercise outdoors. They develop problems when something triggers an exacerbation, such as exposure to an allergen to which they are sensitized, a respiratory infection, or air pollutants, among others. Arguably the most important potential adverse effect of acute ozone exposure in a child with asthma is not whether it causes a transient decrement in lung function, but whether it causes an asthma exacerbation.

2. Ozone has respiratory effects beyond its well-described effects on lung function. It increases airway inflammation, a key component in the pathophysiology of asthma. Eosinophilic inflammation is particularly important in allergic asthmatics, and we know from clinical studies that airway eosinophilia is increased in response to ozone exposure in asthmatics. Ozone increases non-specific airways hyperresponsiveness in clinical studies. And ozone exposure causes airway epithelial injury and increases airway epithelial permeability, both cardinal features in asthma pathophysiology. This increases the potential for materials deposited in the distal airways, such as particles or allergens, to access the lung interstitium and vascular space. These effects beyond lung function decrements likely contribute to the risk of an asthma exacerbation. Yet they are not captured or considered in the risk analysis.

EPAs current approach minimizes/ignores the full spectrum of potential ozone airway effects. The human clinical studies indicate that both lung function decrements and increased airway inflammation result from exposures as low as 60 ppb in the 6.6-hr studies. The focus in the risk assessment is solely on FEV_1, because that database is robust. But we know from other studies that the FEV_1 response and the airway inflammatory response occur via different mechanisms [2-4], and some people are more prone to one of these effects than the other. This means that there are individuals who will experience increases in airway inflammation without lung function decrements or symptoms. The absence of symptoms could result in a failure of the individual to limit exposure, thereby further worsening the airway inflammatory effect of the exposure.

It is reasonable to expect that, in people with asthma, an increase in airway inflammation is an adverse effect, with the potential to increase the risk for an asthma exacerbation. Repeated episodes of airway inflammation may enhance airway remodeling, which occurs in asthma, and leads to irreversible reductions in lung function.

Studies in smokers provide additional evidence that adverse respiratory effects of ozone can occur in the absence of lung function decrements. Current active smokers are generally unresponsive to the lung function decrements of ozone exposure [5], but still may experience airway inflammation [2], and may be at risk for increased oxidative stress effects, because their alveolar macrophages are primed by the smoking [6].

3. The ozone PA makes the following **assumptions**:

a. Lung function decrements in response to 7-8 hour exposures near 70 ppb are the same in asthmatic children as they are in healthy adults.

The clinical data in people with mild to moderate asthma, exposed at higher concentrations than those directly relevant to the standard, suggest that asthmatics do not have markedly increased FEV_1 declines compared with healthy subjects. But it is inappropriate to assume that this extends to lower concentrations, or to people with more severe disease. Asthmatics do appear to experience greater effects on measures of airway obstruction, including airways resistance testing. This is briefly reviewed in the ISA, but not considered in the risk assessment. None of the low-concentration, 6 to 7 hr studies listed in Tables 3A-1 and -2 included asthmatics. And very few clinical studies have included severe or even moderate asthma, let alone asthmatic children. And none have included unstable asthmatics or those prone to exacerbations. This is a key knowledge gap, and raises legitimate questions about whether the current standard provides an adequate margin of safety for people with asthma.

b. Absence of symptoms means less adversity.

The PA seems to suggest that lung function decrements in the absence of symptoms do not represent an adverse health effect. But this should not apply to children with asthma.

c. Lung function and other respiratory effects are rapidly reversible in asthmatic children, similar to healthy adults.

The time course of the pulmonary function response is well established in healthy adults, but less well in children, and especially in children with asthma. We have no data on the persistence of respiratory effects in asthmatics following low-concentration, more prolonged exposures.

4. The current ozone NAAQS level of 70 ppb does not provide an adequate margin of safety for children with asthma.

The EPA focuses almost exclusively on lung function effects in its risk assessment because of the abundant human data on that measurement. The databases for ozone effects on airway inflammation, nonspecific airway hyperresponsiveness, airway epithelial injury, and epithelial permeability are much more limited than for lung function responses, in part because of greater challenges in measurement. However, the current analysis ignores the possibility, and in fact the likelihood, that transient lung function decrements may not be the most adverse effect of ozone exposure, especially for people with abnormal airways at baseline, as in asthma or COPD. We know from the clinical studies, cited in the ISA and the PA, that 0.60 ppb ozone exposure for 6.6 hrs with exercise increases airway inflammation (in addition to causing lung function decrements) in healthy people. Airway inflammation and other effects need to be considered in the risk assessment because of their relevance in chronic lung disease, especially asthma. The exposure analysis tells us that up to 11% of asthmatic children will experience exposures of this magnitude in areas that just meet the current standard of 70 ppb. We don't know with any certainty how many of those children would/will experience worsening of their asthma as a consequence. But the clinical rationale supporting such a risk is compelling. The epidemiological studies, despite their remaining uncertainties, support this concern. It therefore seems clear that a

NAAQS level of 0.70 ppb does not provide an adequate margin of safety, especially for people with airways disease such as asthma.

CASAC recognized this in its advice to the EPA during the 2014 review:

"The CASAC advises that, based on the scientific evidence, a level of 70 ppb provides little margin of safety for the protection of public health, particularly for sensitive subpopulations. In this regard, our advice differs from that offered by EPA staff in the Second Draft PA. At 70 ppb, there is substantial scientific evidence of adverse effects as detailed in the charge question responses, including decrease in lung function, increase in respiratory symptoms, and increase in airway inflammation. Although a level of 70 ppb is more protective of public health than the current standard, it may not meet the statutory requirement to protect public health with an adequate margin of safety. In this regard, the CASAC deliberated at length regarding advice on other levels that might be considered to be protective of public health with an adequate margin of safety. For example, the recommended lower bound of 60 ppb would certainly offer more public health protection than levels of 70 ppb or 65 ppb and would provide an adequate margin of safety. Thus, our policy advice is to set the level of the standard lower than 70 ppb within a range down to 60 ppb, taking into account your judgment regarding the desired margin of safety to protect public health, and taking into account that lower levels will provide incrementally greater margins of safety.
[Letter from H. Christopher Frey, CASAC Chair, to Gina McCarthy, EPA Administrator, dated June 26, 2014, p. ii, https://yosemite.epa.gov/sab/sabproduct.nsf/5EFA320CCAD326E885257D030071531C/%24File/EPA-CASAC-14-004+unsigned.pdf.]
Based on what we know about ozone respiratory effects presented in the ISA, and what we know about the nature of asthma, CASAC's advice in 2014 appears to be relevant for the current review.

Additional Comments

P. 3-50 line 7: Rather than "assessing exposure, ventilation rate, intake dose, and estimated health risk", suggest "estimating exposure, ventilation rate, ozone intake, and health risk".

In the ISA, EPA has established a new health effect category of both short and long-term metabolic effects, each with a "likely" causality categorization, but has not included these effects in the risk assessment. This is most likely due to the difficulties in performing risk assessment without much evidence from human clinical or observational studies. The reasons for the absence of such a risk assessment should be at least briefly addressed in the PA.

P. 3D-80. For the MSS model, lung function decrements are assumed to be 0 for age >55 yrs. This model does not incorporate newer data on lung function effects in healthy older subjects [7], which demonstrated lung function effects in subjects older than 55 yrs. This should be acknowledged in the PA.

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Dr. Ronald Kendall

The Clean Air Scientific Advisory Committee (CASAC) has been asked to review the document, "Policy Assessment for the Ozone National Ambient Air Quality Standards, External Review Draft" submitted October 31, 2019. The document will be referred to as 2019 Draft IRP and Ronald J. Kendall was assigned Chapter 4 – Review of the Secondary Standard and the charge was as follows:

> *Chapter 4 – Review of the Secondary Standard: What are CASAC views on the approach described in Chapter 4 to considering the evidence for welfare effects in order to inform preliminary conclusions on the Secondary Standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the Secondary Standard?*

Background on the Current Standard

The current Standard was set in 2015 based on the scientific and technical information available at that time as well as the Administrator's judgements regarding the available welfare effects evidence, the appropriate degree of public welfare protection for the revised Standard, and available air quality information on seasonal cumulative exposures that may be allowed by such a Standard (80 FR 65292, October 26, 2015). With the 2015 decision, the Administrator revised the level of the Secondary Standard for photochemical oxidants, including ozone (O_3) to 0.070 ppm (70 ppb) in conjunction with retaining the indicator (O_3), averaging time (8 hours), and form (4^{th}-highest annual daily maximum 8-hour average concentration, averaged across three years).

The welfare effects evidence base available in the 2015 Review included decades of extensive research on the phytotoxic effects of O_3, conducted both in and outside of the U.S. that documents the impacts of ozone on plants and their associated ecosystems (U.S. EPA, 1978, 1986, 1996, 2006, 2013).

In light of the extensive evidence base, the 2013 Integrated Science Assessment (ISA) concluded there was a causal relationship between ozone and visible foliar injury, reduced vegetation growth, reduced productivity in terrestrial ecosystems, reduced yield and quality of agricultural crops, and alteration of belowground biogeochemical cycles. In addition, the 2013 Ozone ISA concluded there was likely to be a causal relationship between O_3 and reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial ecosystem water cycling, and alteration of terrestrial community composition (2013 ISA). Further, based on the then available evidence with regard to O_3 effects on climate, the 2013 Ozone ISA also found there to be a causal relationship between changes in tropospheric ozone concentrations and radiative forcing, found there likely to be a causal relationship between tropospheric ozone concentrations and effects on climate as quantified through surface temperature response, and found the evidence to be inadequate to determine if a causal relationship exists between tropospheric ozone concentrations and health and welfare effects related to UV-B shielding (2013 ISA).

The 2015 Decision was a public welfare policy judgment made by the Administrator, which drew upon the available scientific evidence for O_3-attributable welfare effects and on analyses of exposures and public welfare risks based on impacts to vegetation, ecosystems and their associated services, as well as judgements about the appropriate weight to place on the range of uncertainties inherent in the evidence and analyses.

Considerations Regarding Adequacy of the Prior Standard

The Administrator's conclusion in the 2015 Review regarding the adequacy of the Secondary Standard that was set in 2008 (0.075 ppm, as annual 4th-highest daily maximum 8 hour average concentration averaged over three consecutive years) gave primary consideration to the evidence of growth affects in well-studied tree species and information in cumulative seasonal ozone exposures in certain study areas. In doing so, the exposure information for Class I areas was evaluated in terms of the W126 Cumulative Seasonal Exposure Index, an index recognized by the 2013 ISA as a mathematical approach "for summarizing ambient air quality information in a biologically meaningful form for ozone vegetation effects purposes" (2013 ISA). The EPA focused on the W126 index for this purpose consistent with the evidence of the 2013 ISA and advice from the Clean Air Scientific Advisory Committee (CASAC). The Administrator gave particular weight to analysis with focus on exposures in Class I areas, which are lands that Congress set aside for specific uses intended to provide benefits to the public welfare, including lands that are to be protected so as to conserve the scenic value and the natural vegetation and wildlife within such areas and to leave them unimpaired for the enjoyment of future generations. This emphasis on lands afforded special government protections such as national parks and forests, wildlife refuges, and wilderness areas, some of which are designated as Class I areas under the Clean Air Act, was consistent with a similar emphasis in the 2008 Review of the Standard (73 FR 16485, March 27, 2008).

As noted across past reviews of the Ozone Secondary Standard, Administrator's judgments regarding effects that are adverse to public welfare consider the intended use of the ecological receptors, resources, and ecosystems affected. Thus, in the 2015 Review, the Administrator utilized the median RBL estimate for the studied species as a quantitative tool within a larger framework of considerations pertaining to the public welfare significance of O_3 effects. The Administrator recognized such considerations to include effects that are associated with effects on growth and that the 2013 ISA determined to be causally or likely causally related to ozone and ambient air, yet for which there are greater uncertainties affecting estimates of impacts on public welfare. These other effects included reduced productivity in terrestrial ecosystems, reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial community composition, alteration of below ground biogeochemical cycles, and alteration of terrestrial ecosystem water cycles. The Administrator in considering the revised lower standard, noted that a revised Standard would provide increased protection for other growth-related effects, including for relative yield loss (RYL) of crops, reduced carbon storage and for types of effects for which it is more difficult to determine public welfare significance, as well as for other welfare effects of ozone, such as visible foliar injury (80 FR 65390, October 26, 2015).

In reaching a conclusion in the amount of public welfare protection from the presence of ozone and ambient air that is appropriate to be afforded by a revised Secondary Standard, the Administrator gave particular consideration to the following:

1. The nature and degree of effects of O_3 on vegetation,
2. The strength and limitations of the available and relevant information,
3. Comments from the public on the Administrator's proposed decision, and
4. The CASAC reviews regarding the strength of the evidence and its adequacy to inform judgements on public welfare protection.

It was also noted that the Clean Air Act does not require that a Secondary Standard be protective of all effects associated with a pollutant in the ambient air, but rather those known or anticipated effects judged "adverse to the public welfare" (CAA Section 109).

Does the Current Evidence Alter Conclusions from the Last Review Regarding the Nature of Welfare Effects Attributable to O_3 in Ambient Air?

The evidence newly available in this Review supports, sharpens, and expands on the conclusions reached in the last Review (Draft Ozone ISA, Appendices 8 and 9). Consistent with the evidence in the last Review, the currently available evidence describes an array of ozone effects on vegetation and related ecosystem effects as well as the role of ozone in radiative forcing and effects on temperature, precipitation, and related climate variables. Evidence newly available in this review augments more limited previously available evidence related to insect interaction with vegetation, contributing to conclusions regarding ozone effects on plant-insect signaling (Draft Ozone ISA, Appendix 8) and on insect herbivores (Draft Ozone ISA, Appendix 8). Thus, the conclusions reached by EPA in the last Review are supported by the current evidence base and conclusions are reached in a few new areas based on the now expanded evidence. The 2019 Ozone PA details of effects of ozone on vegetation and ecosystem processes are reviewed in detail and updated with newly available evidence.

Public Welfare Implications

The public welfare implications of the evidence regarding ozone welfare effects are dependent on the type and severity of the effects, as well as the extent of the effect at a particular biological or ecological level of organization. In the Draft Ozone PA, EPA discusses such factors in light of judgements and conclusions made in prior reviews regarding effects on the public welfare. As provided in Section 109 (b) (2) of the Clean Air Act, the Secondary Standard is to "specify a level of air quality the attainment and maintenance of which in the judgement of the Administrator…is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air". The Secondary Standard is not meant to protect against all known or anticipated ozone related welfare effects, but rather those that are judged to be adverse to the public welfare in a bright line determination of adversity it is not required in judging what is requisite. Thus, the level of protection from known or anticipated adverse effects to public welfare that is requisite for the Secondary Standard is a public welfare policy judgement to be made by the Administrator.

Is There Information Newly Available in this Review Relevant to Consideration of the Public Welfare Implications of Ozone Related Welfare Effects?

The categories of effects identified in the Clean Air Act to be included among welfare effects are quite diverse and, among these categories, any single category includes many different types of effects that are of broadly varying specificity and level of resolution. For instance, effects on vegetation is a category identified in the Clean Air Act Section 302 (h), and the 2019 Ozone ISA recognized numerous vegetation related effects of ozone at the organism, population, community, and ecosystem level (Draft ISA, Appendix 8). In the decisions to revise the Secondary Standard in the last two reviews (2008, 2015) the Administrator recognized that by providing protection based

on consideration of effects in natural ecosystems in areas afforded special protection, the revised Secondary Standard would also "provide a level of protection for other vegetation that is used by the public and potentially affected by ozone including timber, produce grown for consumption and horticultural plants used for landscaping" (80 FR 65403, October 26, 2015). EPA provides in the Ozone PA figure 4-2. Potential effects of O_3 on the public welfare, which does an excellent job at summarizing the potential effects of causal or likely to be causal impact of ozone on vegetation at the organism, population, community, and ecosystems levels.

Exposures Associated with Effects

The types of effects identified in Figure 4-2 of the Ozone PA vary widely with regard to the extent and level of detail of the available information that describes the ozone exposure circumstances that may elicit them. Therefore, EPA organized a section in the 2019 Ozone PA to address first, effects of ozone exposure on growth and yield effects, a category of effects for which information on exposure metrics and E-R relationships is most advanced. In addition, EPA discusses the current information available regarding exposure metrics and relationships between exposure and the occurrence and severity of visible foliar injury.

Growth Related Effects

The longstanding body of vegetation effects evidence includes a wealth of information on aspects of ozone exposure that are important in influencing effects on plant growth and yield (Draft 2019 ISA). A variety of factors have been investigated, including "concentration, time of day, respite time, frequency of peak occurrence, plant phenology, predisposition, etc.," (2013 Ozone ISA). In the last several reviews, based on the then available evidence, as well as advice from the CASAC, the EPA has focused on the use of cumulative, seasonal concentration-weighted index for considering the growth related effects evidence and in quantitative exposure analyses for purposes of reaching conclusions on the Secondary Standard. More specifically, the EPA used the W126-based cumulative, seasonal metric (Draft 2019 ISA). This metric, commonly called the W126 Index, is a non-threshold approach described as the sigmoidally weighted sum of all hourly ozone concentrations observed during a specified daily and seasonal time window, where each hourly ozone concentration is given a weight that increased from 0-1 within increasing concentration (2013 ISA). The most well studied data sets in this regard are those for 11 tree species seedlings and ten crops referenced and described by Lee and Hogsett (1996) and Hogsett et al (1997). These datasets include 1) for growth effects on seedlings of a set of tree species and 2) for quality and yield effects of a set of crops. These datasets, which include growth and yield response information across a range of multiple seasonal cumulative exposures, were used to develop robust, quantitative, E-R functions for reduced growth (termed Relative Biomass Loss or RBL). In seedlings of the tree species and E-R functions for RYL for a set of common crops (Draft 2019 ISA, Appendix 8) the EPA's conclusions regarding exposure levels of ozone associated with vegetation related effects at the time of the last review were based primarily on these established E-R functions. The 2019 Ozone Draft ISA concludes that "the cumulative exposure indices, including the W126 Index, "are the best available approach for studying the effects of ozone exposure on the vegetation in the U.S." (Draft 2019 Ozone ISA, Appendix 8). Accordingly, in this review, the EPA as in the last two reviews used the seasonal W126-based cumulative, concentration-weighted metric for consideration of the effects evidence

in quantitative exposure analyses, particularly related to growth effects, which appears reasonable and scientifically sound. This information for the tree species, in combination with air quality analysis was a key consideration in the 2015 EPA decision on the level for the revised Secondary Standard (80 FR 65292, October 26, 2015).

Other Effects

With regard to climate related effects, including radiative forcing, the newly available evidence in this review does not provide more detailed quantitative information regarding ozone concentrations at the national scale. Although ozone continues to be recognized as having a causal relationship with radiative forcing and a likely causal relationship with effects on temperature, precipitation, and related climate variables, the non-uniform distribution of ozone (spatially and temporally) makes the development of quantitative relationships between the magnitude of such effects in differing ozone concentrations in the U.S. challenging (Draft 2019 Ozone ISA, Appendix 9). Thus, the Draft 2019 Ozone ISA recognizes that "current limitations in climate modeling tools, variation across models, and the need for more comprehensive observational data on these effects represents sources of uncertainty in quantifying the precise magnitude of climate responses to ozone changes, particularly at regional scales (Draft 2019 Ozone ISA). While these complexities affect EPA's ability to consider specific ozone concentrations associated with differing magnitudes of climate-related effects, it does give EPA the ability to estimate growth-related impacts of trees that can inform their consideration of the sequestration of carbon in terrestrial ecosystems, a process that can reduce tropospheric abundance of the pollutant (CO2) ranked first in importance as a greenhouse gas and radiative forcing agent.

What Are Important Uncertainties in the Evidence?

Among the categories of effects identified in past reviews, key uncertainties remain in the current evidence (Draft Ozone PA 2019). The category of ozone welfare effects for which current understanding of quantitative relationships is strongest is reduced plant growth. As a result, this category was the focus of the Administrator's decision making in the last review, with RBL in tree seedlings playing the role of surrogate for the broader array of vegetation related effects that range from the individual plant level to ecosystem services. Limitations in the evidence base and associated uncertainties recognized in the last review remain and include a number of uncertainties that affect characterization of the magnitude of cumulative exposure conditions eliciting growth reductions in U.S. forests.

As recognized in the last review, there are uncertainties in the extent to which the 11 tree species for which there are established E-R functions encompass the range of ozone sensitive species in the U.S. and also the extent to which they represent U.S. vegetation as a whole. Therefore, it should not be assumed that species of unknown sensitivity are tolerant to ozone.

EPA recognized important uncertainties in extent to which the E-R functions for reduced growth in tree seedlings are also descriptive of such relationships during later life stages for which there is a paucity of established E-R relationships. In addition, EPA recognizes limitations and their ability to estimate growth effects of tree lifetimes of year to year variation in ozone concentrations. For

example, the studies on which the established E-R functions for 11 tree species are based vary in duration (such as 82 days in a single year to 555 days spanning more than one year). In the 2019 Draft Ozone PA, EPA goes to great lengths in walking through uncertainties and recognizing limitations and data interpretation with a number of studies that they have considered. This is not unexpected due to the biological variability in response to a pollutant such as ozone in ecological systems.

Exposure and Air Quality Information

In general EPA decision making in the last review placed greatest weight on estimates of cumulative exposures to vegetation based on ambient air monitoring data for ozone and consideration of those estimates in light of E-R relationships for ozone related reduction in tree seedling growth. These analyses supported the consideration of the potential for ozone effects on tree growth and productivity as well as its associated impacts on a range of ecosystem services, including forests, ecosystem productivity, and community composition (80 FR 65292, October 26, 2015).

In revising the Standard in 2015 to the now current Standard, the Administrator concluded that with revision of the Standard level, the existing form and averaging time provided the control needed to achieve the cumulative seasonal exposure circumstances identified for the Secondary Standard. The focus of cumulative seasonal exposure primarily reflects the evidence of E-R relationships for plant growth. The 2015 conclusion was supported by the air quality data analyzed at that time. Analysis in the 2019 current review of the still more expanded set of air monitoring data, which includes 1,545 monitoring sites with sufficient data for variation of design values, documents similar findings as from the analysis of data from 2000 -2013 described in the last review.

Monitoring sites with lower ozone concentrations as measured by the design value metric (based on the current form and averaging time of the Secondary Standard) also have lower cumulative seasonal exposures, as quantified by the W126 Index. As the form and averaging time of the Secondary Standard have not changed since 1997, the analyses performed have been able to assess the control exerted by these aspects of the standard in combinations with reductions in the level (i.e., from 80 ppb in 1997 to 75 ppb in 2008 to 70 ppb in 2015) on cumulative seasonal exposures in terms of the W126 Index.

In the 2019 Draft Ozone PA in Figure 4-7, W126 Index values at monitoring sites with valid design values (2015-2017) the evidence currently available leads EPA to conclusions regarding exposure levels associated with effects as similar conclusions in the last review. Based largely on this evidence in combination with use of RBL as a surrogate, for vegetation related effects, the value of 17 ppm–hrs was the average W126 Index (over three years) was identified in the 2015 decision (80 FR 65393; October 26, 2015). As summarized above, the information available in the present review continues to indicate that cumulative seasonal exposure levels at virtually all sites with air quality meeting the current standard fall below the level of 17 ppm-hrs that was identified when the current standard was established (80 FR 65393; October 26, 2015). Additionally, the average W126 Index in Class I areas that meet the current standard for the most recent three year period is below 17 and at or below 13 ppm-hrs in 44 of those of 46 Class I areas. In addition, in the current draft 2019 Ozone PA, table 4-2 summarizes distribution of W126 Index values in/near Class I areas. In summary, as is the case at all monitoring sites nationally, sites in or near Class I areas with design values at or below

70 ppb in the most recent three year period have had a seasonal W126 Index (based on three year average) at or below 17 ppm-hrs. As was the case at the time the current standard was established, with the exception of four values that occurred nearly a decade ago in the southwest region, cumulative seasonal exposures in all Class I areas during periods that met the current standard were no higher than 17 ppm-hrs which reflects a protective level in the standard.

Based on established E-R functions for tree seedling growth reductions in 11 species, the tree seedling RBL for the median tree species is 5.3% for a W126 Index of 17 ppm-hrs, rising to 5.7% for 18 ppm-hrs, 6% for 19 ppm-hrs and 6.4% for 20 ppm-hrs. Below 17 ppm-hrs, median estimates include 4.9% for 16 ppm-hrs, 4.5% for 15 ppm-hrs, 4.2% for 14 ppm-hrs, and 3.8% for 13 ppm-hrs. These estimates are unchanged from what was indicated by the evidence in the last review.

EPA has focused in the current review on the E-R relationships available in the last review for purposes of considering ozone exposure levels associated with growth-related impacts. Currently available evidence, including the newly available in the 2019 Ozone Draft ISA does not indicate the occurrence of ozone-related effects attributable to cumulative ozone exposures lower than was established at the time of the last review (.07 ppm). As in the last review, the currently available evidence continues to support a cumulative, seasonal exposure index as a biologically-relevant and appropriate metric for assessment of the evidence of exposure/risk information for vegetation, most particularly for growth related effects. This is reasonable, responsible, and reflects good use of scientific information by the EPA. The evidence continues to support important roles for cumulative exposure and for weighting higher concentrations over lower concentrations of ozone and ambient air. Thus, among the various such indices considered in the literature the cumulative, concentration-weighted W126 function continues to be best supported for purposes of relating ozone air quality to growth-related effects.

The RBL appears to be appropriately considered as a surrogate for an array of adverse welfare effects and based on consideration of ecosystem services and potential for impacts to the public as well as conceptual relationships between vegetation growth effects and ecosystem scale effects. Biomass loss is a scientifically sound surrogate of a variety of adverse effects that could be exerted to public welfare. In the previous review, the Administrator used RBL as a surrogate for consideration of the broader array of vegetation related effects of potential welfare significance that included effects of growth of individual sensitive species and extended to ecosystem level effects such as community composition in natural forests, particularly in protected public lands (80 FR 65406, October 26, 2015). EPA believes, and I concur, that information available in the present review does not call into question this approach, indicating there continues to be support for the use of tree seedling RBL as a proxy for the broader array of vegetation-related effects, most particularly those related to growth.

<u>To What Extend Does the Available Information Alter Our Understanding of the Magnitude of Growth Reductions Expected to be of Public Welfare Significance?</u>

It was recommended in the last review that a 6% RBL was “unacceptably high” and endeavored to identify a Secondary Standard that would limit three year average ozone exposures somewhat below W126 Index values associated with a 6% RBL in the median species. This led to identification of a seasonal W126 Index value of 17 ppm-hrs that the Administrator concluded appropriate as a target at

or below which the new Standard would generally restrict cumulative seasonal exposures (80 FR 65407, October 26, 2015). The currently available evidence continues to indicate conceptual relationships between reduced growth and the broader array of vegetation-related effects of ambient ozone exposure.

What Does the Information Available in the Current Review Indicate with Regards to Support for Use of a Three Year Average Seasonal W126 Index as the Cumulative Exposure Metric (Associated with a Value of 17 ppm-hrs) for Describing the Requisite Level of Protection for the Secondary Standard?

In the setting of the current Standard, the EPA focused on control of seasonal cumulative exposures in terms of a three year average W126 Index metric. The evaluations in the PA for the last review recognized there to be limited information to discern differences in the level of protection afforded for cumulative growth related effects by a Standard focused on a single year W126 as compared to a three year W126 Index (80 FR 65390, October 26, 2015). Accordingly, the identification of the three year average for considering the seasonal W126 Index recognized that there was year-to-year variability, not just in ozone concentrations, but also in environmental factors, including rainfall and meteorological factors, that influences the occurrence and magnitude of ozone related effects in any year and contribute uncertainties to interpretation of the potential for harm to public welfare over the longer term. Based on this recognition, as well as other considerations, the Administrator expressed greater confidence in judgements related to public welfare impacts based on seasonal W126 Index estimated by a three year average and accordingly relied on that metric, which appears of reasonable thought and scientifically sound.

Does the Currently Available Scientific Evidence in Air Quality and Exposure Analyses Support or Call into Question the Adequacy of the Protection Afforded by the Current Secondary Ozone Standard?

As delineated by the Clean Air Act, the Secondary Standard is meant to protect against ozone related welfare effects that are judged to be adverse to the public welfare. The EPA in development of the Draft 2019 Ozone PA considered the currently available information regarding welfare effects of ozone in this context, while recognizing that the level of protection from known or anticipated adverse effects to public welfare that is requisite for the Secondary Standard is a public welfare policy judgement made by the Administrator. EPA considered the quantitative analyses, including associated limitations and uncertainties and the extent to which they indicate differing conclusions regarding the level of protection indicated to be provided by the current Standard from adverse effects. EPA additionally considered the key aspects of the evidence in air quality/exposure information emphasized in establishing the now current Standard and the associated public welfare policy judgements and judgements about inherent uncertainties that are integral to decisions on the adequacy of the current Secondary Ozone Standard. In considering the currently available evidence, EPA recognized the long-standing evidence base of the vegetation-related effects of ozone, augmented in some aspects since the last review. Consistent with the evidence in the last review, the currently available evidence describes an array of ozone effects on vegetation and related ecosystem effects as well as the role of ozone in radiative forcing with effects on climate related variables. The current evidence base supports conclusions of causal relationships between, particularly, vegetation and other endpoints and likely to be causal relationships between other endpoints that EPA thoroughly discussed in the 2019 Draft ISA. EPA appropriately recognized uncertainties in

categories of effects newly identified that could limit consideration of the protection that might be provided by the current Standard against these effects.

As was the case in the last review, a category of effects for which the evidence supports quantitative description of relationships between air quality conditions and response is plant growth or yield. The evidence base continues to indicate growth-related effects as sensitive welfare effects, with the potential for ecosystem scale ramifications. For this category of effects, there are established E-R functions that relate cumulative seasonal exposure of varying magnitudes to various incremental reductions in expected tree seedling growth (in terms of RBL) and in expected crop yield. Decades of research also recognizes visible foliar injury as an effect of ozone, although uncertainties continue to hamper efforts to quantitatively characterize the relationship of its occurrence and relative severity with ozone exposures.

Reviews of NAAQS also required judgements on the extent to which particular welfare effects (such as with regard to type, magnitude/severity, or extend) are important from a public welfare perspective. In the case of ozone, such a judgement includes consideration of the public welfare significance of small estimates of RBL and associated unquantified potential for larger scale effects. With regard to public welfare significance of 5-6% RBL, the EPA notes CASAC characterization of 6% RBL (in seedlings of median tree species) in the last review. The rationale provided by the CASAC with this characterization was primarily conceptual and qualitative rather than quantitative. The conceptual characterization recognized linkages between effects on the plant level scale and broader ecosystem impacts, and this facilitated the Administrator consider RBL as a surrogate for the broader impacts that could be elicited by ozone. In the 2015 decision, the Administrator took note of CASAC advice regarding use of RBL as a proxy and set the Standard with "underlying objective of a revised Secondary Standard that would limit cumulative exposures in nearly all instances to those for which the median RBL estimate would be somewhat lower than 6%" (80 FR 65407, October 26, 2015). The 2015 decision noted that "the Administrator does not judge RBL estimates associated with marginal higher exposures [at or above 19 ppm-hrs] in isolated rare instances to be indicative of adverse effects to the public welfare" (80 FR 65407, October 26, 2015).

In considering the quantitative analyses available in the draft 2019 Ozone PA, EPA noted the findings from the analysis of recent air quality at sites across the U.S., including in or near 64 Class I areas and also analysis of historical air quality. Findings from the analysis of air quality data from the most recent period and from the larger analysis of historical air quality data extended back to 2000 are consistent with the air quality analysis findings that were part of the basis for the current Standard. That is, in virtually all design value periods and in all locations at which the current Standard was met, the three year average W126 metric was at or below 17 ppm-hrs, the target identified by the Administrator in establishing the current Standard (80 FR 65404-65410, October 26, 2015).

EPA summarized in the draft 2019 Ozone PA there is little in the information available in the current review that differs from that in the last review that relate to key aspects of the judgments and associated decision that established the current Standard in 2015. The new information available is consistent with that available in the last review for the principle effects for which the evidence is strongest (such as growth, reproduction, and related larger scale effects, as well as visible foliar injury).

General Comments

1. I compliment the United States Environmental Protection Agency on a very thorough and well-written Chapter 4 contributing to the draft 2019 Ozone Policy Assessment.
2. The foundation upon which scientific data was utilized while also incorporating concepts of judgement on behalf of the EPA with input from various entities lays a strong and clear scientific process of considerations for the preliminary conclusions on the current Secondary Standard.
3. The preliminary conclusion by the U.S. EPA that the 2015 decision to revise the level of the Secondary Standard for photochemical oxidants, including ozone to .07 ppm (70 ppb) in conjunction with retaining the indicator (O_3), averaging time (8 hours) and form (4^{th} highest annual daily maximum 8-hour average concentration, averaged across three years) appears to be working in maintaining ambient air concentrations of ozone across the United States at levels that are protective for the public welfare, particularly as related to vegetation.
4. EPA recommends the RBL appears to be appropriately considered as a surrogate for an array of adverse welfare effects and based on consideration of ecosystem services and potential for impact to the public as well as conceptual relationships between vegetation growth effects and ecosystem scale effects. I agree that biomass loss, as reported in RBL, is a scientifically sound surrogate of a variety of adverse effects that could be exerted to public welfare.
5. EPA believes, and I concur, that information available in the present review does not call in to question this RBL approach, indicating there continues to be support for the use of tree seedling RBL as a proxy for the broader array of vegetation related effects, most particularly those related to growth that could be impacted by ozone.
6. It was recommend in the last review that a 6% RBL was "unacceptably high" and endeavored to identify a Secondary Standard that would limit three year average ozone exposure somewhat below W126 Index values associated with a 6% RBL in the median species, and I concur that this strategy is still scientifically reasonable. The identification of a seasonal W126 Index value of 17 ppm-hrs that EPA concludes appropriate as a target at or below which the Secondary Standard would generally restrict cumulative seasonal exposure. I believe that this target is still effective in particularly protecting the public welfare in light of vegetation impacts from ozone.
7. The approach described in Chapter 4 to considering the evidence for welfare effects is laid out very clearly, thoroughly discussed and documented, and provided a solid scientific underpinning for the preliminary conclusions leaving the current Secondary Standard in place.

Dr. Sabine Lange

A reference list can be found at the bottom of this document for those studies that are not referenced in the ozone PA.

Charge Questions: Chapter 3 – Review of the Primary Standard: What are the CASAC views on the approach described in chapter 3 to considering the health effects evidence and the risk assessment in order to inform preliminary conclusions on the primary standard? What are the CASAC views regarding the key considerations for the preliminary conclusions on the current primary standard?

Air Quality

The EPA states in section 3.1.2.2 that "Analyses described in detail in the HREA suggested that reductions in O3 precursors emissions in order to meet a standard with an 8-hour averaging time, coupled with the appropriate form and level, would be expected to reduce O3 concentrations in terms of the metrics reported in epidemiologic studies to be associated with respiratory morbidity and mortality (80 FR 65348, October 26, 2015)."

However, multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time, over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. My general summary from the consultant responses to this point is that decreasing peak ozone concentrations will not consistently decrease the mean ozone concentrations and therefore one cannot expect to improve the metrics associated with respiratory mortality and morbidity in epidemiology studies (driven by the mean) by reducing the ozone standard (which targets the peak).

Health Effects Evidence and Risk Assessment

Accurate & Balanced Reporting

There are a few places in this document that require some editing to ensure fully accurate and balanced reporting of data and analyses.

In several places the EPA summarizes the the causality designations as: "The current evidence primarily continues to support our prior conclusions regarding the key health effects associated with O3 exposure." (Section 3.3.1, Section 3.5.1). This is not an accurate summary statement, because there have been some substantial changes in the causality determinations since the last review. Those changes are described in the paragraph following this sentence, and so this initial statement needs to be changed to more accurately reflect that.

In section 3.3.1.1 the EPA states that "Evidence regarding respiratory infections and associated effects has been augmented by a number of epidemiologic studies reporting positive associations between short-term O3 concentrations and emergency department visits for a variety of respiratory infection

endpoints (draft ISA, Appendix 3, section 3.1.7.4)." Section 3.1.7.4 of the ISA also shows a number of studies that do not report positive associations between ozone and infections - the EPA needs to consider how to report these and other epidemiology results in a more balanced manner.

Fully Justified Conclusions

There are a few places in this document that require some editing to ensure that the EPA has fully supported the conclusions that are being drawn.

In section 3.3.1.2 (Other Effects), the EPA does not adequately explain why the evidence for metabolic effects is likely causal, when they state that the data is mostly from animal studies with high exposure levels and there is limited concordance with human epidemiology studies with some contradictory evidence. Similar with long-term exposure and metabolic effects.

In section 3.3.3, the EPA notes in reference to experimental animal results of respiratory effects that "The exposures eliciting the effects in these studies included multiple 5-day periods with O3 concentrations of 500 ppb over 8-hours per day (draft ISA, section 3.2.4.1.2)." This type of information should be considered for biological plausibility, not just when deciding on relevant concentrations for risk assessment.

Additional Policy-Relevant Information

There are some areas where additional information could be added to help provide information to decision makers. In Section 3.3.2 the EPA could add what fraction of the population (particularly at-risk populations if possible) are expected to spend 6.6 hours or more outdoors at moderate exertion. This information would help decision makers compare the exposure likelihood to the primary CHE studies.

In section 3.5.1 (Evidence-based considerations) the EPA notes that "The current evidence does not alter our understanding of populations at risk from health effects of O3 exposures." However, what about the new metabolism causality determination? Does this suggest that people who are obese or have metabolic syndrome are more susceptible?

Study Limitations

In section 3.3.3 the EPA states that "We have also considered what may be indicated by the epidemiologic studies regarding exposure concentrations associated with health effects, and particularly by such concentrations that might occur in locations when the current standard is met. In so doing, however, we recognize that these studies are generally focused on investigating the existence of a relationship between O3 occurring in ambient air and specific health outcomes, and not on detailing the specific exposure circumstances eliciting such effects" And "these studies generally do not measure personal exposures of the study population or track individuals in the population with a defined exposure to O3 alone. Notwithstanding this, we have considered the epidemiologic studies identified in the draft ISA as to what they might indicate regarding O3 exposure concentrations in this regard." It is good that the EPA acknowledged this limitation with these studies. Consistent with the recommendations from the expert consultants, these caveats should be applied to all similar air pollution epidemiology studies, not just those for ozone.

Clarity of Presentation

There are a few places in this document that require some editing to ensure that data and analyses are clearly reported.

In section 3.4.2 (Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard) and elsewhere the EPA refers to the population exposure estimates (i.e. the estimates of percent of the population exposed to certain concentrations of ozone) as a risk estimate. On its surface, these estimates appear to be exposure, rather than risk, estimates. The EPA should clarify their definitions of risk and exposure for readers.

The EPA presents quite different risk estimates from the MSS and E-R models. These are discussed at length in Appendix 3D, with an in-depth justification of the choice of the E-R model risk results over the MSS results. The EPA should add more of this information to the main text to clarify further to the reader why they emphasize the E-R model results over the MSS results.

The EPA states that "The limited evidence that informs our understanding of potential risk to people with asthma is uncertain but indicates the potential for them to experience greater effects or have lesser reserve to protect against such effects than other population groups under similar exposure circumstances, as summarized in section 3.3.4 above." It is not the case that the limited evidence indicates the potential for people with asthma to experience greater effects, although it is true and logical that they may have less reserve. These two aspects need to be discussed separately and the differences noted, because the ways in which they are taken into account are different. For the former, you assume that people with asthma have a steeper E-R response, or a lower threshold (although there is little data to suggest that this is the case). For the latter, you use a lower adverse effect threshold, as the EPA already does with the 10% FEV1 decrement threshold.

In section 3.4.5 (Public Health Implications), I suggest adding a summary of the percent of children with asthma experiencing a 10% FEV1 decrement, with a sentence or two about the adversity of those changes in lung function.

Quantitative Uncertainty Analysis

The EPA does not provide uncertainty bounds on their exposure or risk estimates. The ranges presented represent variability between cities, not uncertainty. There are many ways that some measure of uncertainty can be accounted for in these estimates, some of which are discussed and presented in the Appendix – these should be included in the main text to provide the Administrator with this information for decision making. For example, on page 3D-145, the EPA references Glasgow and Smith 2017, a study that provides a method for quantitative uncertainty evaluation. There is also an upper bound estimate of the ER function that is presented in Table 3D-64 – if there was an upper and lower bound function provided, then those could simply be used for some quantification of uncertainty for the exposure-response model.

The EPA discusses uncertainties with air quality analysis in section 3.4.4 (Key Uncertainties) as well as the ways in which they have tried to reduce this uncertainty. However, this type of uncertainty is a prime

candidate for a quantitative uncertainty analysis because there are estimates on the uncertainties associated with the air quality estimates.

In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." The EPA should provide a rationale for assuming a lack of threshold in an exposure-response relationship as a way of considering potential at-risk populations that may not have been characterized in an exposure-response assessment. As per the expert consultant responses it is not clear that this is a validated assumption for models based on CHE study data.

Risk Threshold

The EPA states in section 3D.2.8.2.2 that the McDonnell-Stewart-Smith (MSS) model has a threshold of accumulated dose built into the model. The EPA notes that this is not a concentration threshold and does not preclude effects at lower concentrations. However, it is a threshold that suggests (as has been suggested by other models (Schelegle et al., 2012) and is consistent with the known MOA of ozone in the respiratory tract) that there are ozone doses below which no effects are expected to occur. This concept of threshold should be discussed by EPA in the main text and should be considered as a factor that is incorporated into the E-R model.

Other Notes

In the Appendices in a number of locations there is "Error Reference Not Found!" - these need to be located and fixed.

In section 3.3.1.1 Footnote: "As recognized in section 3.3.1.1 above, the single newly available 6.6-hour study is for subjects aged 55 years of age or older, and has a slightly lower target ventilation rate for the exercise periods. The exposure concentrations were 120 ppb and 70 ppb, only the former of which elicited a statistically significant FEV1 decrement in this age group of subjects (draft ISA, Appendix 3, section 3.1.4.1.1.2)." This was a typo I think - the Arjomandi study was a 3-hour exposure, not a 6.6 hour exposure.

The end of the second bullet point on page 3-51 is cut-off mid sentence.

The last sentence of the first paragraph on page 3-82 needs to be edited - there seem to be words missing or juxtaposed.

There is a figure (referenced in page 3D-91) that seems to be labeled as "0", instead of with the figure name.

Questions to Consultants

1) *Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time,*

over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are your thoughts about the change of annual average ozone concentrations (which tend to be the focus of epidemiology studies) with decreases in annual peak ozone concentrations?

Responses:

Dr. Jaffe: "Yes, I agree with your statements: Annual averages have changed much less than the design values due to the NOx disbenefit. How this impacts health is a question for epidemiologists, so I am not able to answer."

Dr. Jansen: "While there may be exceptions, I would expect any changes in the annual averages to be small and could go in either direction. One question I would ask is what the epidemiological studies do when the monitors do not operate for the full year, which is the case of most monitors."

Dr. Lipfert: "I used the data for two frequency distributions from Figure 1 to estimate how cumulative risks could depend on the exposure-response function (ERF) threshold. I postulated a linear ERF so that the contribution to the total risk is the product of the frequency and the midpoint of the O3 concentration bin (Figure 2). With no threshold or up to about 30 ppb, there is no difference in cumulative risk, as is the case with high thresholds (> 80 ppb). In the mid-range (thresholds from 40-80 ppb), the cumulative risk for the higher design value (DV) distribution is about double that of the lower one while the ratio of the 2 DVs is only 1.3, showing the importance of thresholds. Most epi studies have used some measure of peak O3 rather than the annual average. My own studies (see Appendix) have used the 95th percentile of the daily O3 averages."

Dr. North: "I fully agree that the decrease in annual average ozone exposure is significant. I continue to have concerns on whether the epidemiological results imply manipulative causality as opposed to association, and I am pleased to read that EPA is not using these epidemiological results but rather basing its recommendations (for the last round and the present one) mainly on human clinical studies. There are still areas of the US, such as the Sacramento area, that have MDA8 levels well above the current standard of 70 ppb. I would like to see CASAC focus on the public health risk in these areas. See my general comments above regarding asthma. There ought to be more research to see if high ozone episodes in Sacramento (and elsewhere in the Central Valley and the Los Angeles to San Diego area) have led to increases in hospital admissions and emergency department visits."

Dr. Parrish: "The general situation exemplified in Figure 1 is more or less typical of the temporal evolution of urban ozone concentration distributions, where maximum daily 8-hour average (MDA8) ozone concentrations have decreased, but the minimum MDA8 values have increased. This causes the distribution of MDA8 ozone concentrations to narrow, as shown in the figure. The cause of the increase in the minimum MDA8 ozone concentrations is a reduction in fresh NO emissions in the urban area. The effect of these emissions on days of low photochemical activity is for NO to react with ozone, forming NO2. Thus, between the early 2001-2003 period and the later 2013-2015 period, on days of low photochemical activity the MDA8 ozone concentrations have increased but the NO2 concentrations have decreased. Since the mean and median MDA8 have not changed significantly over this time interval, it may well be that the annual average ozone concentrations have not changed much. The possibility that annual average ozone concentrations have not changed, but that NO2 concentrations have decreased,

would be important to consider in the interpretation of epidemiology studies that focus on annual average ozone concentrations."

Dr. Sax: "EPA does acknowledge that "Reductions of NOX emissions are expected to result in a compressed O3 distribution, relative to current conditions" (Draft Ozone PA, pg. 2-4), and it looks like that is what is shown in Dr. Lang's Figure 1. As Figure 1 shows, however, this also means that there will be more days that experience somewhat higher ozone concentrations, although potentially no days with levels that exceed very high concentrations. With regards to how these changes should be interpreted for epidemiology studies, I think the larger issue of how ambient levels relate to actual personal exposures of ozone and how this impacts exposure measurement error in the epidemiology studies is a more critical issue. In the PA, EPA acknowledge this important source of uncertainty, and is one reason provided for not conducting the "epidemiology- based" risk assessment."

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2) *Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?*

Responses:

Dr. Jansen: "I am not a statistician but I do not see how it could "protect against" confounding etc. Confounding exists or it doesn't. If one tests for confounding then maybe the higher statistical power allows it to be demonstrated more reliably."

Dr. Lipfert: "No; sample size only affects random error. Effects of measurement error, incomplete control of confounders, or a miss-specified model are independent of sample size. Cohort analyses are widely regarded as the best approach to studying long-term effects, but cohort sample size can only be increased by recruiting more subjects or extending follow-up time, which entails aging and loss of the more susceptible subjects."

Dr. North: "No. I responded to a similar question in the O3 ISA. Statistical power comes from having a large sample size, and NOT from having resolved issues of confounding, error, and bias. Consider we have a study of 10 million children showing that shoe size predicts reading ability. Because data were obtained from 10 million children, a very large number, the confidence interval is quite narrow. Does this apparently accurate prediction imply that getting children larger shoes will improve their reading ability? No way!"

Dr. Sax: "The issue of statistical power is separate from issues related to confounding, errors and bias. You can have a very large study that has serious confounding issues if these are not controlled for (or are unmeasured). Similarly, large studies can be prone to selection bias, exposure measurement errors, etc. Sample size (or statistical power) will affect whether you are able to "detect" an effect, and is only one aspect of study quality (larger sample sizes are preferred), but is separate from other issues of study quality, which are associated with the study design, execution, and analyses methodology. That is, poor study design, execution or poor methodology can lead to errors and biases."

Dr. Thomas: "No. Sources of selection, information, and confounding biases could potentially affect any study, irrespective of sample size (or power). That said, very large studies conducted by highly experienced investigators generally make every effort to address such problems in the design and analysis and would discuss these issues in their publications. Also, studies of individual-level data may have access to more information to address bias than meta-analyses or aggregate-level studies."

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3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40[1] and pg 3-43[2]). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?*

Responses:

Dr. Jansen: "Yes, I believe those statements to be correct. I believe the statements are generally true and the caveat should apply generally, not to just ozone. I suspect the reason it is highlighted here in the ozone proceeding is because ozone concentrations may be more variable than, say, PM among micro-environments. Exposure is very dependent on the integrated levels of ozone in those micro-environments, thus the use of the highly complex and data intensive APEX model. That said, it is not clear that why similar efforts are not done for PM and the other NAAQS. Studies have shown differences in PM and their species between the ambient and homes, restaurants, groceries, etc. In many cases PM is higher indoors due to numerous sources (e.g., cooking, dust, pet dander). Note that indoor sources of ozone (e.g., air purifiers) were explicitly excluded in this assessment. I find it curious that EPA expends so much effort with APEX on ozone and not PM. Finally, the whole APEX discussion implies but does not demonstrate that the complexities added to APEX result in a more accurate exposure estimate."

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[1] "We have also considered what may be indicated by the epidemiologic studies regarding exposure concentrations associated with health effects, and particularly by such concentrations that might occur in locations when the current standard is met. In so doing, however, we recognize that these studies are generally focused on investigating the existence of a relationship between O3 occurring in ambient air and specific health outcomes, and not on detailing the specific exposure circumstances eliciting such effects."

[2] "As associations reported in the epidemiologic analyses are associated with air quality concentration metrics as surrogates for the actual pattern of exposures experienced by study population individuals over the period of a particular study, the studies are limited in what they can convey regarding the specific patterns of exposure circumstances (e.g., magnitude of concentrations over specific duration and frequency) that might be eliciting reported health outcomes."

Dr. Lipfert: "Yes, this is correct in all cases. Epidemiology deals only in numbers, not rationales. Reduced lung function may lead to hospitalization and then to death, but individual longitudinal analyses would be required to follow such a path. Each of these processes would require its own long-term analysis with its own confounders to be controlled and it is possible, perhaps likely, that different pollutants could be involved in each process (except for smoking). I know of no epidemiology studies that link sequential long-term effects. The time-series model of Murray and colleagues (see Appendix) postulates a frail subpopulation from which all daily deaths emanate in response to spikes in air pollution and/or temperature. An advanced version of this model solves for prior relationships with air pollution or temperature but the corresponding time scales are uncertain. This model decouples the causes of frailty from the causes of daily mortality which are likely to differ. Studies of daily mortality and hospital admissions have indicated similar relationships with ozone, but longer-term studies have not."

Dr. North: "I am inclined to think that the problem is a general one that will only be resolved by getting data on potential confounders such as income (more generally, socioeconomic status), and extremes of temperature, which have large impacts on mortality and morbidity via mechanisms independent of air pollutants. However, we should understand that at VERY high exposure levels, air pollutants such as ozone and fine particulate matter (e.g., smoke) can cause illness and death. The shape of the exposure-response relationship is critical for assessing the risks. Extrapolation over orders of magnitude is readily done with available mathematics. But how this extrapolation is done should reflect judgment on the biological mechanisms underlying damage to health."

Dr. Sax: "I agree with this statement – the ambient data, whether from fixed-site monitors or from modeling data are only surrogates of the actual personal exposures and any differences contribute to exposure measurement errors. This statement is true for all air pollution studies, not only ozone, and this caveat should be included for other air pollution epidemiology studies."

Dr. Thomas: "The two statements cited are generally correct and apply broadly to air pollution epidemiology studies, not just ozone. Most epidemiologic studies are based on measurements of ambient pollution levels, which are readily available. For some pollutants, indoor sources or penetration from outdoor sources, local variation in pollutant concentrations, time-activity patterns, etc., can be important sources of inter-individual variation, which some studies have attempted to quantify by, for example, personal monitoring, microenvironmental measurements, exposure modeling, GPS or accelerometer instruments, etc., but such studies are expensive and may be infeasible for large-scale epidemiologic studies. Since the statements queried do apply to ozone studies, I don't see than any particular caveats are needed to point out the generality of this issue."

Exposure-Response Modeling

4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an*

exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?

Responses:

Dr. Lipfert: "I'm not aware of any "standard methods" for dealing with thresholds, aside from controlled (clinical) experiments that are sensitive to selection of subjects. A linear relationship may be the default option with noisy data for which the lowest concentrations may be the least reliable. However, there are good reasons to accept the concept of (essentially) zero threshold, that differ between long- and short-term analyses. The time-series model of Murray and colleagues analyzes daily mortality relationships in terms of the combination of subject frailty and air pollution. Death may result from excess frailty or excess pollution or both. As a result, in a sufficiently large population there will likely always be someone sick enough to succumb to a small air pollution perturbation; the threshold depends on the population at risk. The situation with long-term effects is more complicated. They result from cumulative or repeated exposures after a period of latency, so that effects of pollution abatement will be delayed and it becomes difficult to define the appropriate exposure over the periods involved. Background ozone will also play a role. Here the threshold depends on the characteristics of exposure. Finally, health responses during a year will be the result of both long-and short-term exposures, so that even in the absence of long-term effects there may be pollution-related mortality at any outdoor concentration level. Also, different pollutants may be involved at different time scales."

Dr. North: "Yes, assuming a lack of threshold has become a standard method in many areas of EPA's risk assessment practice. Many of us old-timers believe this practice is questionable, because absence of evidence is not evidence of absence. The biological mechanisms underlying the adverse health response should be assessed based on available information including judgment. Traditional toxicology has used a sigmoid shaped exposure-response function, on the basis that very small exposures (episodic or cumulative) are unlikely to trigger an adverse response but as the exposure increases, the body's defenses and repair mechanisms can become inadequate, so the adverse effect becomes common in an exposed population. And the response may saturate with most or all of those who are susceptible to it having the adverse response – e.g., given enough bacteria in the spoiled food, nearly everyone gets sick from eating it. But linearity to zero became common in cancer risk assessment. This assumption was originated as a health-protective default assumption for screening: a plausible upper bound for identifying chemicals deserving more detailed risk analysis, and not for estimating the incidence of human cancer. But linear to zero is often used for the latter purpose."

Dr. Sax: "This approach does not make sense to me. If asthmatics are truly more susceptible to the effects of ozone, then it might be that the threshold for effects might be lower, but not zero. Although data are limited, the data that are available do not indicate that asthmatics are more susceptible than non-asthmatics to the effects of ozone. In fact, data are inconsistent, with some studies indicating effects in asthmatics at elevated ozone exposures, but others showing no effects. For example, no effects on lung function were observed in asthmatics compared to non-asthmatics at exposures to 400 ppb for 2 hours (Alexis et al., 2000) and 200 ppb for 2 hours (Mudway et al., 2001)."

Dr. Thomas: "As I pointed out in earlier rounds of questions, the exact shape of a dose-response relationship at low doses, including the existence or not of a threshold, is difficult if not impossible to determine from feasible-sized epidemiologic studies. Hence, the default analysis model generally

assumes low-dose linearity (or log-linearity depending on the form of the outcome variable); see for example the classic paper by Crump, Hoel, Langley, and Peto (1976) I previously cited. This would be true for either main effects in the whole population or for effect modification in potentially sensitive subpopulations, to the extent that the necessary data on individuals are available. The question of effects below the current standard is particularly important, and especially for highly sensitive groups; to the extent that such data exist, any demonstrable low-dose associations should be considered in revising the standard, whether or not the assumption of low-dose linearity or thresholds can be tested."

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5) *The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?*

Responses:

Dr. Lipfert: "Most epidemiology studies assume a homogeneous population at risk which may be convenient but is unrealistic. The remaining life expectancies of those aged 65 and over range from one day to 35 y or more with a median around 15 y. (This situation pertains for populations but not necessarily cohorts, depending on subject selection.) Many air pollution epidemiology studies have shown higher risks for subjects with pre-existing conditions. Lung cancer mortality rates are proportional to the cumulative cigarettes smoked, even though not all smokers get lung cancer. Following this model, we would expect air pollution-related mortality to respond to cumulative exposures from a few days to decades, depending on many other variables including preexisting disease. The answer to this question is thus: Yes, air pollution epidemiology includes all degrees of susceptibility but the most highly susceptible subjects may dominate the group response."

Dr. North: "I am concerned that FEV1 decrements are not a good indicator for adverse health impacts in sensitive populations. (See my general comments at the beginning of this response. FEV1 measurements vary a good deal. The Belzer-Lewis paper mentioned in my O3 ISA response has perceptive criticism about using FEV1 data in research.) It seems to me that lack of information, referring to the words you use in your first sentence, (1) should motivate detailed studies of the people that are judged to be at highest risk, and (2) leaders of agencies such as EPA should think beyond legally required standard setting to the bigger issue of how to protect public health with an adequate margin of safety. If adverse health effects are judged to be essentially absent for much of the United States (a reasonable inference from Figure ES-1 in the ISA and Figure 2-5, page 2-12 in the PA), then attention should be focused on the remaining areas where such adverse health effects may still be occurring. Are these adverse health impacts really there in these remaining areas, or are our government officials being overly precautionary and protective in setting standards, but ignoring major public health protection needs by assuming that some causes, such as wildfires, are "natural background?" EPA should be using common sense and not be trapped in traditions that violate common sense. The levels of ozone and fine particulate matters that millions of people in California have experienced from wildfire smoke plumes in 2017, 2018, and 2019

are far above the NAAQS standards and pose serious health effects, especially to members of sensitive subgroups. Some of these people are among my family, my friends, and my neighbors. The costs involved in reducing these risks to health from wildfire plumes are very large. So are the costs of bringing ozone levels in Sacramento into compliance with a 70 ppb MDA8 standard, even if with wildfire periods are exempted. (In my humble judgment, the former activity makes much more sense than the latter.) EPA staff and CASAC should acknowledge these facts in their written documents, as part of advising the EPA Administrator on strategy with respect to criteria air pollutants. I believe giving such advice is within the legal mandate of CASAC under the Clean Air Act."

Dr. Sax: "The controlled human exposure studies that form the basis of the exposure-response model are based on exposure circumstances that are highly unlikely to occur in the general population, and in particular in susceptible population groups (i.e., heavily exercising individuals exposed to elevated concentrations of ozone over extended periods of time). Only outdoor workers are likely to experience the exposure conditions in these studies. In addition, the results clearly indicate that only a small percentage of the study volunteers (although generally healthy adults) had a statistically significant response to ozone, and as noted by Dr. Lange, these responders likely represent people that are more susceptible to ozone (particularly at lower ozone concentrations). Therefore, I agree that the model already represents a very conservative estimation of ozone effects that are likely to be protective of sensitive population groups."

Dr. Thomas: "This question appears to relate more to controlled human exposure studies than to epidemiologic studies but does seem to be a reasonable approach for getting a handle on inter-individual variability in susceptibility in that context. Obviously, the slope of an exposure-response relationship in the general population will underestimate risk for more sensitive individuals, or more importantly, for identifiable subgroups. Of course, there are other characteristics than lung function (e.g., genetic variants, age/gender, baseline health status, etc.) that could influence sensitivity of ozone or other pollutants. To the extent that the necessary data are available, most epidemiologic studies have reported variation across quantifiable subgroups, and given EPA's mandate to provide adequate protection to such groups as well as to the entire population should be taken into consideration in revising standards."

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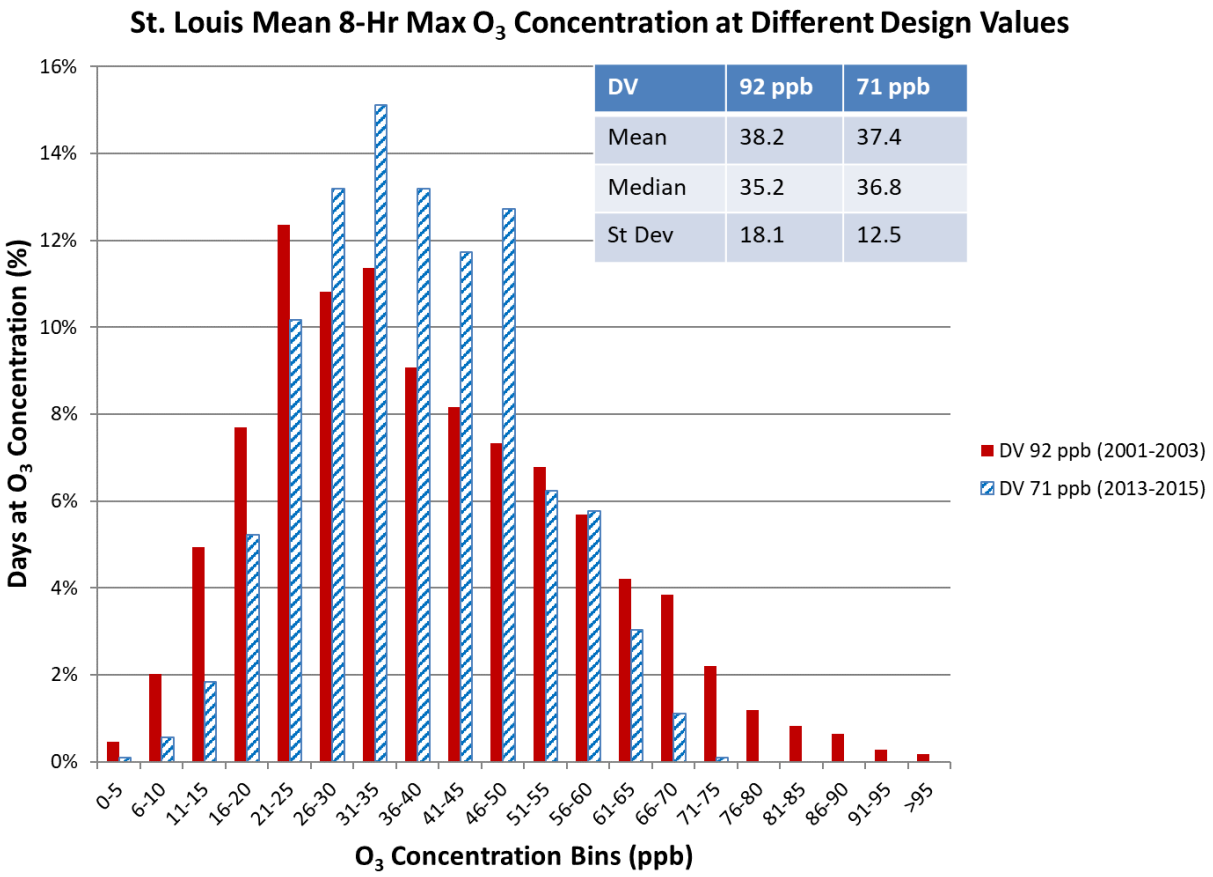


Figure 1. Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV – design value.

Dr. Corey Masuca

Chapter 2 – Air Quality

2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks

There is a noticeable absence of discussions about Near Road monitoring sites, especially for NOy, as an ozone precursor.

2.3.2 Data Handling Conventions and Computations for Determining Whether the Standards Are Met

More elucidation needs as to why the selection of the ozone design value as the 3-year average of the annual 4th highest daily 8-hour maximum concentration.

2.5 Background Ozone

While this section focuses on background concentrations, expressed as concentrations that would exist in the absence of US anthropogenic emissions and ozone concentrations from global natural sources and from anthropogenic sources transports from sources outside of the US, what localized, interstate and/or intercity transport of anthropogenic ozone and/or precursors?

Chapter 3 - Review of the Primary Standard

3.3.1.2 – Other Effects

With respect to the determination that metabolic effects have been determined to have likely causal relationship with ozone exposures, should this finding stand even though the evidence the most salient evidence is from animal studies at exposure conditions much higher than those commonly occurring?

3.3.2 Public Health Implications and At-Risk Populations

With respect to at-risk populations, there appears to be a noticeable absence of discussion about greater susceptibility for minority and/or lower SES populations.

3.3.3 Exposure Concentrations Associated with Effects

This section indicates that otherwise valid epidemiological studies (US and Canada) which found positive associations between ozone and respiratory outcomes were deemed to be less useful since the studies were conducted in areas and during time periods that would not have met the current standard.

When evaluating epidemiological health effects, should this limitation be placed on study and study result effectiveness? In other words, should epidemiological evidence **only** be limited to those areas that

meet the current standard with disregard for effects noted as both higher and lower concentrations that those of the current standard?

3.4 Exposure and Risk Information

General Questions

What is the inherent purpose of the risk assessment in the policy assessment evaluation?
Are the results from the risk assessment viewed to be more substantive than controlled human and epidemiological studies? Even given the extensive list of uncertainties highlighted in 3.4.4

3.4.1 Conceptual Model and Assessment Approach

For the risk assessment, why the utilization of ambient air monitoring data consisting of concentrations at or near the current standards? Why not consider ozone concentrations well above and below the current standard also?

3.4.2 Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard

While not totally invalid, some concern with developing risk estimates from concentrations from eight (8) representative cities.

Greater explanation and concern with 'simulated children with asthma.'

While the focus has been on areas just meeting the current standard, how would the percentages change for each benchmark (i.e., 60 ppb, 70 ppb, 80 ppm) for concentrations below the current standard? For concentrations above the current standard?

3.5.2 Exposure/Risk-Based Considerations

While not totally invalid, some concern with developing risk estimates from concentrations from eight (8) representative cities.
While the focus has been on areas just meeting the current standard, how would the number of days and lung function decrement changes for concentrations below the current standard? For concentrations above the current standard?

Dr. Steven Packham

Preliminary Comment. Empirical observations and pulmonary function data from controlled human exposures are sufficient to conclude that a causal biological mechanism exists between objectively measured decrements in FEV1 and subjective symptoms in healthy human adults.

1. The shape of the biologically mediated FEV1 dose-response curve is a function of the inhaled hourly dosage rate and the cumulative dose inhaled over several hours immediately prior to the onset of the effect.
2. The threshold for these biologically mediated FEV1 responses in healthy adult humans exposed for 6.6 hours to ozone concentrations from 60 to 87 ppb is estimated to be 1,362 µg. (Schelegle et al. 2009)
3. This is equivalent to a cumulative dose of millions of trillions of highly reactive oxidizing molecular moieties.

Formula 1. $\frac{1362\mu g}{48gm} \cdot AvogadroN = 1.709 \times 10^{19}$

4. The threshold doses for ozone induced FEV1 and reports of symptomatic effects are lower than for clinical signs of pulmonary inflammation.
5. Ozone induced FEV1 decrement is most probably one of several specific protective biological responses.
6. Ozone exposures have been shown to stimulate peripheral mucus flow into central bronchi thereby enhancing particle transport from peripheral to central airways and mucociliary clearance of inhaled particulate matter.
7. This beneficial dose-dependent response to ozone "…is of interest since it characterizes the reaction of a primary defense mechanism essential to the protection of mucosal surfaces of the tracheobronchial tree." (Forster et al. 1987)

Recommendations. In order to present a review of key scientific studies and an integration of current scientific evidence and knowledge, future O3 ISA and PA documents MUST present a clear description of all the known biological mechanisms underlying the O3-FEV1 effect and further validate and refine the dose response functions for FEV1 and pulmonary inflammation derivable from controlled human exposure studies.

In response to the Question,
"When a causal relationship is conclusive to a high degree of scientific certainty as it is in this case, should this take precedence over causal inference when drafting a NAAQS ISA?" Dr. Parrish Responded:

> I have no relevant expertise, so I cannot respond to this question as an expert; however, to a non-expert the answer is obviously, Yes.

Substantive-bases for these Recommendations. Figure ES-3 in the Ozone ISA External Review Draft (shown below) is adapted from the 2013 Ozone ISA which was based on eight

human studies published between 1988 and 2013. The 2009 study by Schelegle et al. specifically played a decisive role in the 2015 revision of the O3 NAAQS from 75 to 70 ppb (80 FR 65292 Oct 26, 2015).

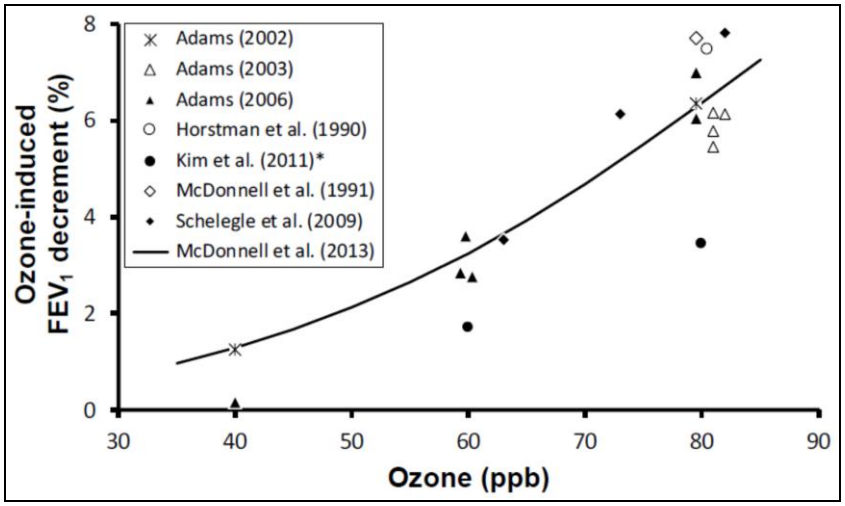


Figure ES-3 was adapted from **Figure 6-1 of 2013 Ozone ISA (U.S. EPA, 2013)** which was based on studies by Adams (2006), Adams (2003), Adams (2002), Folinsbee et al. (1988), Horstman et al. (1990), Kim et al. (2011), McDonnell et al. (2013), McDonnell et al. (1991), and Schelegle et al. (2009).

In contrast to **Figure ES-3**, the original figure (***Figure 1***) shown below from Schelegle et al. 2009, depicts the actual sigmoid curvilinear relationships and mean accumulative doses of the 31 healthy adult human subjects who completed the four 6.6-hour chamber exposures to target mean O_3 concentrations of 60,70, 80, and 87 ppb.

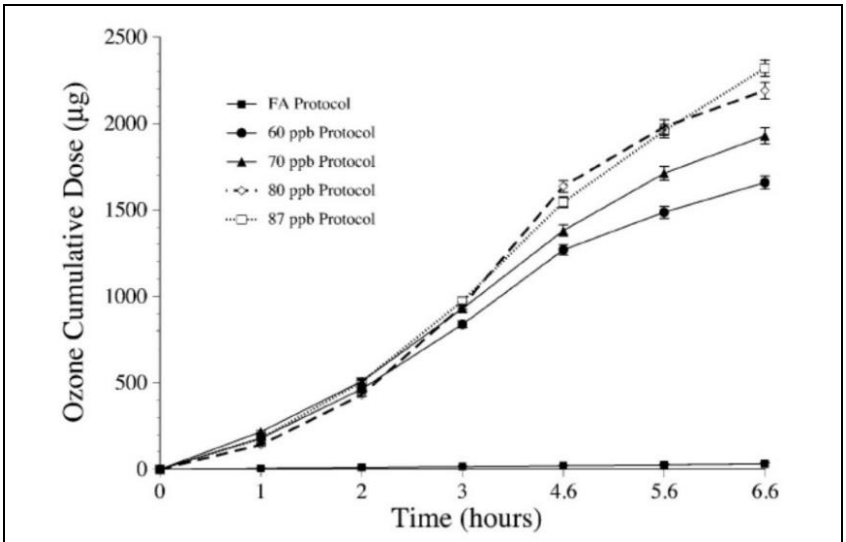
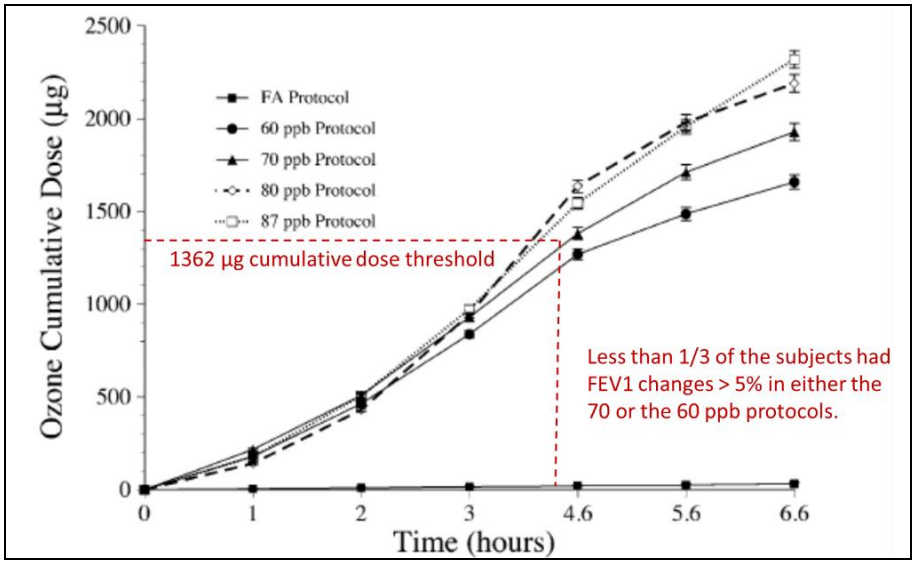


Figure 1. Diagram of mean group values for cumulative dose of ozone (micrograms) against time of exposure for each of the five protocols. Values represent means ± SEM.

The original data presented *in this way* conveys critical information to toxicologists and biomedical researchers that is "lost in translation/integration" in the concentration/risk-effect picture presented in Figure ES-3. To quote Schelegle et al. (2009), "*We were able to obtain reliable estimates of a Dose of Onset [i.e., a threshold for the FEV1 effect], using the pooled FEV1from the 80 and 87 ppb ozone exposure protocols, …but not from the pooled FEV1 data from the 60 and 70 ppb ozone exposure protocols. The inability to estimate [a threshold] using the FEV1 data from the 60 and 70 ppb ozone exposure protocols is most likely because <u>less than one third</u> of the subjects had changes in FEV1 <u>greater than 5%</u> in either of these protocols.* (Emphasis added)



Packham Figure 1. Adapted from Schelegle et al. (2009) with toxicological annotations by author, 2019.

The notable differences between **Figure ES-3** compared with **Packham Figure 1** are driven by how data are interpreted by different scientific disciplines. By superimposing Schelegle's descriptive narrative of conclusions onto the sigmoid shaped dose-response curves, one sees the beginning of an increased trend of dose-response curve separation between hour 3 and hour 4: Indicative of the cumulative Dose of Onset threshold between the respective exposure protocols.

Figure ES-3 is the product of imposing a *quantal* risk-assessment mindset upon data collected from ***continuously graded biological responses*** characteristic of the ongoing physical events integral to the nature of living organisms.

The narrative associated with **Figure ES-3** (found on page ES-7) is grossly misleading and completely overlooks the positive confounding health benefit of enhanced PM clearance stimulated by 200 ppb ozone exposures mentioned above.

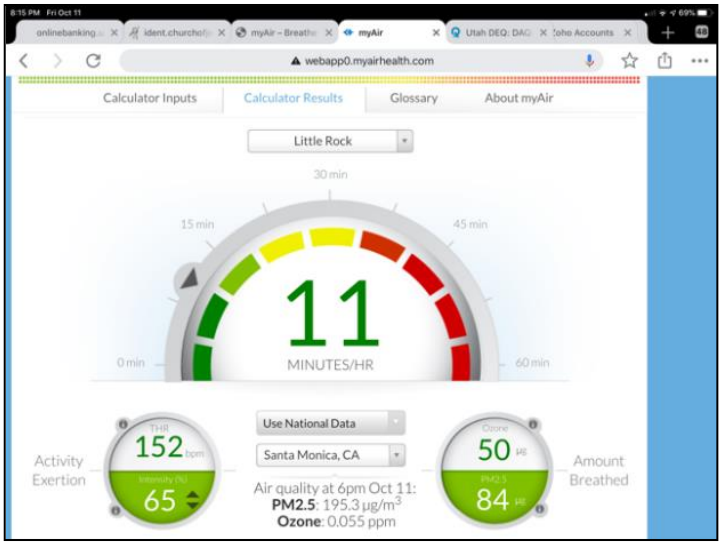
The controlled human studies by Folinsbee, Adams, Horstman, Kim, McDonnell and Schelegle, and others cited below in the References and Reading List, provide the empirical bases of testable hypotheses that exposures to elevated ambient levels of O3 can cause measurable decrements in FEV1 in healthy adults. These studies document that the effect of O3 on reduced FEV1 volumes is temporary and suggest that hourly mean ambient O3 concentrations below 70 ppb are most likely incapable of causing FEV1 effects in most healthy adults.

Pulmonary Physiology and Inhalation Toxicology:
Several nonmember consultants have expressed reluctance to comment on certain questions because of limited familiarity with pulmonary physiology and inhalation toxicology. Here are few facts to keep in mind.

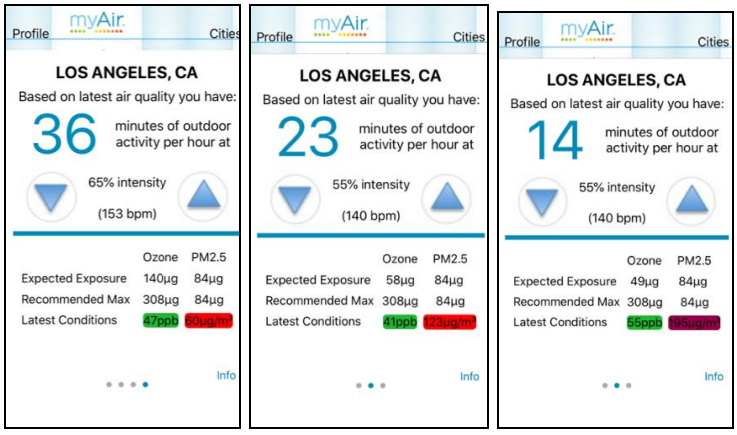
1. Lungs have an evolutionary history in which surfactant was key to the evolution of all air breathing species on the surface of the planet, (Daniels and Orgeig (2003.)
2. Antioxidant secretions from epithelial Type II cells into the liquid lining of the lungs is one of most important natural defenses the human organism has against naturally occurring ozone levels in the atmosphere near the earth's surface.
3. All known effects of ozone on the human respiratory system are dose dependent.
4. Ozone stimulation of the respiratory airways evokes a number of defensive and adaptive physiological responses in humans.

Overarching Health Benefits from Regulations Based on Sound Science: An accurate understanding of the causal dose-response relationship between ambient ozone exposure and responses elicited in the human organism opens up a number of important options that could be considered in reviewing and setting NAAQS standards and in how those standards might be used to protect, and even promote, public health. For instance, the realization that the ozone-induced FEV1 effects are temporary, reversible, and occur at a lower inhaled dose than a potential adverse health effect (such as a pulmonary inflammatory response) could be considered a tenable rationale for classifying them as natural benchmark margin-of-safety indicators.

Another application of minute respiratory volume and hourly MSS inhalation dosage models and thresholds would be for the EPA to imbed them into web and mobile platform applications for public education and personal risk management. Shown here, as proof-of-concept, is a screen shot of such a web application that can be found at http://webapp0.myairhealth.com/# giving an individual (user name Little Rock) in Santa Monica California who is being exposed to 193 µg/m3 of PM2.5 on October 11, 2019 during the Saddleridge wild fire episode the useful information that they should limit any outdoor activity to 11 minutes or less if that activity necessitates a physical exertion intensity level of 65% corresponding to an average heart rate of 152 beats-per-minute or higher.



A free iPhone app is also in the public domain https://apps.apple.com/us/app/myair-health/id790049340. By way of full disclosure, friends and I in Utah developed these web and mobile applications on our own dime and have made them available free to the public since 2013. Here are a few screen shots representative of similar guidance being offered to folks in the Los Angeles area during this same Saddleridge fire episode.



References to these applications in these comments are not being made to announce, promote, or advocate these particular apps; but, to illustrate the power and potential of using sound scientific methods and fundamental principles of toxicology and human respiratory physiology together with current mobile technology to promote public health and demonstrate the public health value inherent in the EPA O3 and PM NAAQS and their associated Air Quality Index Health Advisories when risk assessment and scientific knowledge from controlled human exposure studies are fully integrated.

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Additional Comments

COMMENT 1. Evidence of inflammatory markers induced both by exercise and physical exertion (See list of references in EXHIBIT A) should be included in the final Ozone Policy Assessment (O3 PA) along with a discussion of their effects as potential confounders of inflammatory markers associated with ambient ozone exposure.

COMMENT 2. There needs to be a better presentation of distinctions between a) statistical association versus biological mechanistic concepts of causation, and b) verifiable scientific conclusions versus expert judgments as bases for forming and communicating policy-relevant causal conclusions in the final O3 PA and other documents produced as part of primary NAAQS reviews.

COMMENT 3. The final O3 PA should include a discussion and analyses of potential benefits of alternative forms of the standard on public health (perhaps in Section 3.1.2.3). There was an intriguing idea presented in public comments by the American Thoracic Society (ATS) suggesting that the form of the standard might be modified to provide better health protection through improved risk communication using the air quality index without changing the stringency of the standard benefits. The final O3 PA should also present a review and a quantitative and qualitative analysis of a) the specific standard form alternatives mentioned in public comments by the ATS, and b) other alternatives in the form of the standard that might reasonably be expected to improve compliance with the standard by increasing the opportunity for states and local air quality agencies in development of adaptive management strategies.

COMMENT 4. The first-time I saw *key* studies used to determine the adequacy of a NAAQS was in 1996.[3] In reviewing the three volume PM criteria documentation (CD) as a toxicologist with the Utah Division of Air Quality, I estimated that around 3,885 scientific studies were cited (See TABLE 1). There were at least 390 references on the physical and chemical properties of PM and around 250 references reporting monitoring data of daily and annual background PM concentrations. There were at least 200 references providing data analyses and estimates on human exposure-dose levels and about 500 references on dosimetry and an estimated 500 studies on the toxicity of PM in laboratory animals and controlled human exposures. Nearly 600 references were cited in Volume III on health effects. Most notably, there were only thirty-seven (37) references citing studies of associations between daily PM and mortality. Only four of these studies separated PM effects from the effects of other pollutants and only two were based on data from cities in the United States.

TABLE 1: NUMBER OF CITATIONS RELATING TO SELECTED SUBJECTS IN THE EPA'S, "*Air Quality Criteria for Particulate Matter*."

	Number of Citations
Total	3,885
Number Dealing with:	
Chemical & physical make up of PM	390
Ambient concentrations	250
Estimated human exposure levels	200
Dosimetry	500
Toxicity	500
PM plus other pollutants on mortality	37
PM effects separated from other pollutants	4
PM effects separated: Studies in U. S.	2
PM/mortatlity associations not confirmed	3

[3] United States Environmental Protection Agency. OAQPS Staff Paper. (1996). *Review of the national ambient air quality standards for particulate matter: Policy assessment 0f scientific and technical information*. page VII-2" (EPA Publication No. EPA-452 \ R-96-013). Research Triangle Park, North Carolina: Office of Air Quality Planning and Standards

The impact of these four association studies cannot be overstated; either in the 1996 PM NAAQS review or in all subsequent reviews including the current ozone NAAQS review.

Think of it. Four association studies eclipsed the policy relevance of scientific evidence and knowledge presented from hundreds of laboratory and clinical experiments on living organisms documenting anatomical, biophysical, biochemical and systemic homeostatic defense mechanisms common to humans and other mammalian species against natural and ubiquitous atmospheric stressors such as particulates and ozone. The combined weight of physical evidence reported in hundreds more peer reviewed papers published since 1996 (many of which are not cited in the draft O3 PA) provide a substantive scientific bases for ruling out a likely biophysical mechanism for atmospheric ozone induced mortality in mature mammalian organisms.

COMMENT 5. The EPA should continue to advocate use of association studies in NAAQS reviews; but there are at least two good reasons not to limit itself to the key association study approach. Firstly, it is now conceivable to use heart rate and individual body mass and body surface area, basal metabolism rate and physical exertion levels and local real-time ozone concentrations to calculate personalized respiratory minute volumes and inhaled ozone dose estimates using digital mobile devices. It is now also technically feasible to monitor and collect data from normal and sensitive populations in ad libitum exposure studies involving human volunteers. Such an approach for the collection and analyses of human exposure-response data was not conceivable in 1996. But it is today; and it should be seriously considered by the EPA in future review cycles of ozone and the other criteria pollutants. Secondly, the persistent association study issues of uncertainty and causation can’t be resolved by continuing to focus criteria pollutant policy-relevant assessments on key association studies. “A problem can’t be solved from the same level of consciousness that created it.” (Quote attributed to Albert Einstein.)

EXHIBIT A: References on Inflammatory Markers Induced byExercise and Physical Exertion

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6. Timmons BW, Tarnopolsky MA, Snider DP, Bar-Or O. Immunological changes in response to exercise: influence of age, puberty, and gender. Med Sci Sports Exerc. 2006;38:293–304. [PubMed] [Google Scholar]

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12. Hansen JB, Wilsgård L, Osterud B. Biphasic changes in leukocytes induced by strenuous exercise. Eur J Appl Physiol Occup Physiol. 1991;62:157–161. [PubMed] [Google Scholar]

13. Iatridis SG, Ferguson JH. Effect of physical exercise on blood clotting and fibrinolysis. J Appl Physiol. 1963;18:337–344. [PubMed] [Google Scholar]

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Appendix B

Questions for Non-CASAC Member Consultants on the Draft Ozone PA from CASAC Members

Dr. James Boylan

Chapter 2 – Air Quality

- Is the discussion on O_3 and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Sources and Emissions of O_3 Precursors (Section 2.2) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Background O_3 (Section 2.5) accurate and complete? If not, what additional information needs to be included?

Chapter 3 – Review of the Primary Standard

- Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section 3.4.1) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard (Section 3.4.2) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not, what additional information needs to be included?

Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses

- Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Air Quality Adjustment to Meet Current and Alternative Air Quality Scenarios (Section 3C.5) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Interpolation of Adjusted Air Quality using Voronoi Neighbor Averaging (Section 3C.6) accurate and complete? If not, what additional information needs to be included?
- Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not, what additional information needs to be included?

Dr. Sabine Lange

Air Quality

1) Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time, over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are your thoughts about the change of annual average ozone concentrations (which tend to be the focus of epidemiology studies) with decreases in annual peak ozone concentrations?

Epidemiology

2) Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?

3) In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40[4] and pg 3-43[5]). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?

Exposure-Response Modeling

4) In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?

[4] "We have also considered what may be indicated by the epidemiologic studies regarding exposure concentrations associated with health effects, and particularly by such concentrations that might occur in locations when the current standard is met. In so doing, however, we recognize that these studies are generally focused on investigating the existence of a relationship between O3 occurring in ambient air and specific health outcomes, and not on detailing the specific exposure circumstances eliciting such effects."

[5] "As associations reported in the epidemiologic analyses are associated with air quality concentration metrics as surrogates for the actual pattern of exposures experienced by study population individuals over the period of a particular study, the studies are limited in what they can convey regarding the specific patterns of exposure circumstances (e.g., magnitude of concentrations over specific duration and frequency) that might be eliciting reported health outcomes."

5) The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?

References

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Simon, H., Baker, K., Phillips, S., 2012. Compilation and interpretation of photochemical model performance statistics published between 2006 and 2012. Atmos. Environ. 61, 124–139.

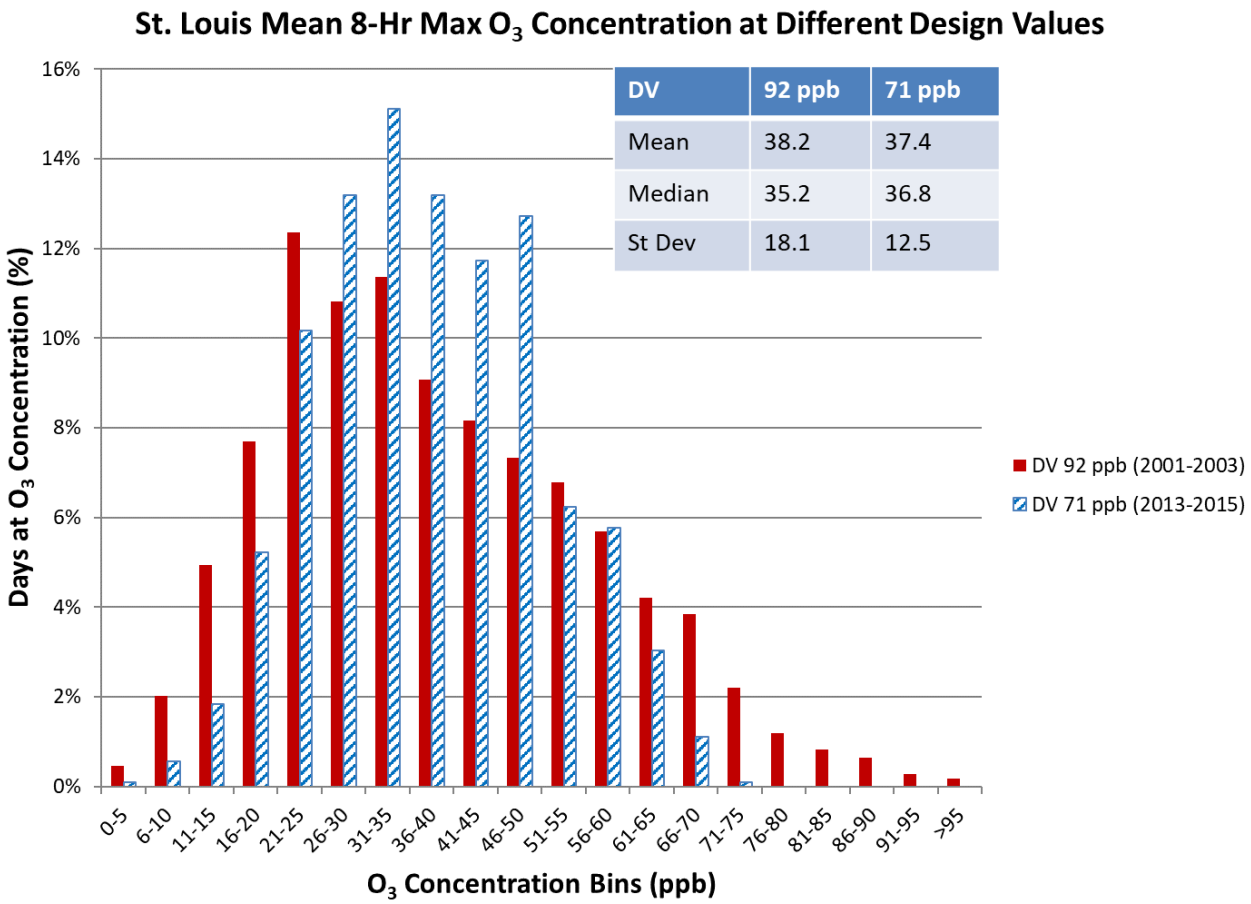


Figure 1. Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV – design value.

Dr. Corey Masuca

1) **2.1. Ozone and Photochemical Oxidants in the Atmosphere**

   How sound science is this mechanism of ozone transfer between the stratosphere and the troposphere?

2) **2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks**

   While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET, National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road Monitoring Sites, especially for NOy?

3) **2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards Are Met**

   There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is this short-term 8-hour rolling average consistent with short-term actual and scientific studies?

4) **2.4.3 Diurnal Patterns**

   While this section refers diurnal patterns of relative ozone concentrations between day and night, are these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant weather conditions? What about the effects on topography/geography in determining diurnal patterns?

5) **Background Ozone**

   There, in general appears to be a lot of discussion about background ozone concentrations from transport and natural sources. However, are most salient ozone concentrations more localized and from anthropogenic sources?

   This section references the utilization of photochemical grid models due to the lack of ability to characterize the origins of ozone and the ability to estimate the magnitude of background ozone. However, how predictable are these photochemical models, especially given the highly photolytic and relative instability of ozone in the atmosphere?

   This section mentions that international emissions sources via transport mostly originate from anthropogenic sources. However, is there a possibility that there can be international transports from non-anthropogenic/biogenic sources?

   Also, this section noticeably leaves out non-international, interstate transport of ozone.

6) 2.5.1.6 Pre-Industrial Methane

There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance of methane with respect to the formation of and consideration of ozone? Is a discussion on methane warranted?

Appendix C

Responses to CASAC Member Questions on the Draft Ozone PA from Non-CASAC Member Consultants

Dr. Dan Jaffe, University of Washington-Bothell

Thank you for the opportunity to assist this round of the NAAQS review.

Response to questions from Dr. Sabine Lange:

1) Yes, I agree with your statements: Annual averages have changed much less than the design values due to the NOx disbenefit. How this impacts health is a question for epidemiologists, so I am not able to answer.

Response to questions from Dr. Corey Masuca:

1) The mechanism for S-T exchange is accurately described. However stratospheric O_3 does not only impact high elevation sites. Its impacts these locations the strongest, but stratospheric O_3 also mixes in and becomes part of the USB.

2) Yes near road monitoring sites should be mentioned. I assume since these data are already included in AQS.

3) I am not following the question. The discussion on the calculation of the MDA8 and design values appears to be correct.

4) Diurnal patterns are controlled by many factors. This includes photochemical production, emissions, temperature and especially meteorology. At night, shallow boundary layers give rise to surface O_3 depletion due to both NO titration and surface reactivity. The discussion mentions most of these factors, except for the role of meteorology and surface deposition.

5) On average, US background contributes about 30 ppb to the total, but there are significant regional, daily and seasonal variations. Thus, background is a significant contributor to O_3 concentrations, even in urban areas. Locally generated O_3 will build on these background concentrations. In general, chemical-transport models have made huge progress in their ability to model O_3 due to improvements in grid resolution, chemistry, meteorology, etc. Nonetheless, there are still uncertainties in the magnitude O_3 on the order of 10 ppb (Jaffe et al 2018). Natural sources (lightning, stratosphere, soil emissions, wildfires,etc) are all included the definition of US background O_3. (see Figure 2-15). Sections 2.5.1 discuss these natural sources. Interstate transport of O_3 would not be considered part of the US background so it would not be discussed in this section. That said it should be mentioned somewhere and I do not see it anywhere in the PA document.

6) As with US background, methane contributes to a global scale enhancement of O_3 of around 5 ppb. Thus it is a small, but significant contribute to urban O_3 everywhere.

Response to questions from Dr. James Boylan:

I have all of section 2 on air quality. Overall I think it is well down and accurately conveys the major sources of surface O_3 in the U.S. I do have the following comments/suggestions:

Page 2-3, line 20: add soils.

Page 2-4, line 9: "volume" ?

Page 2-7, line 23: Really? I don't think a lot of companies are making these instruments yet so when and how will SLAMs implement the chemiluminescent monitoring instruments?

Page 2-18, Figure 2-10: The high elevation site is a bit unusual in showing no diurnal pattern. Typical high elevations sites do show usually show a pattern but can differ from low elevation sites.

Page 2-21, End of section. As noted by Dr. Lange (see her questions), it is also important to discuss changes at the lower end of the distribution and the annual average O_3 associated with changing NOx. It suggests that the overall annual average has not changed much, while the high concentrations have declined.

Page 2-26, line 9: "…global natural AND INTERNATIONAL sources.."

Page 2-27, lines 25+26: I find this sentence confusing.

Page 2-28, line 14: Statement about CO is out of context and maybe misleading.

Page 2-28 line 23: "… are generally small." ??

Page 2-29, lines 1-2: I find the discussion on VOCs a bit simplistic. Not everywhere is swamped by biogenic VOCs. See example in Qian et al 2019 (https://doi.org/10.1021/acs.estlett.9b00160, 2019)

Page 2-29, line 7: Order of magnitude is too large. Maybe factor of 2 or 3.
Page 2-29, line 20: A new analysis by Buysse (DOI: 10.1021/acs.est.9b05241) strengthens this point.

Page 2-29, line 25: The exceptional event rule should also be mentioned here, as it was for strat-trop exchange.

Page 2-32, line 9-10: I think what's important here is the breakdown between natural and anthropogenic methane. We know the current and historical concentrations fairly well.

Page 2-33, line 13: A good references here is Lin 2015 (DOI: 10.1038/ncomms8105)

Page 2-33, line 21: Really need to define "baseline O_3" here.

Page 2-36, line 11: But a lot of the satellite data is associated with the "apriori" which is another model. Do you distinguish based on the fraction of the apriori in the column?

Page 2-37, lines 1-5: This discussion on model errors and bias really needs at least one figure.

Figures 2-16 and 2-17: I think the captions can be improved here. Might be better to say “Modeled MDA8 from all sources and the components”

Figure 2-20: Is there a difference between MDA8 and 8-hour contributions? Also, clarify this is “modeled MDA8”. Can you simplify to “contributions of each sources to the modeled MDA8”.

Figure 2-22: Change “Base ppb” to “total modeled MDA8 ppb”

Page 2-50, line 12: “Error”

Figure 2-25: Hard to read this figure. Suggest focusing on period between May-September.

Figure 2-26: Wrong caption. Suggest focusing on period between May-September.

Page 2-59, line 23: Its probably important out that fire emissions and chemistry are a very large uncertainty, larger than the other natural sources. I also suggest to point out the need for better tools to identify these contributions for exceptional event analyses.

Mr. John J. Jansen, Southern Company (retired)

Given the narrow range of the questions posed by the CASAC members, I read only portions of the draft Ozone Policy Assessment (Chapters 1, 2, 3, Appendix 3C, & portions of Appendix 3D). I have responded to most of the CASAC member questions and also offer some general comments.

General Comments

For the most part I will not repeat comments made on the draft ISA but many of them apply to this document as well. For example, on page 2-3, implying mobile NOx is largely responsible for decreasing NOx emissions ignores substantial reductions in EGU NOx.

I continue to be concerned over the lack of a quantitative integrated uncertainty analysis (IUA) both in individual sections as well as overall for the risk numbers presented. Instead, EPA conducts a qualitative analysis by characterizing "the magnitude and direction of the influence on the assessment for each of these identified sources of uncertainty" page 3D-135 (see also pages 3-64 and 3D-87). The document mentions this qualitative approach several times in the document without any "results" being presented nor a reference to where they are (i.e., Table 3D-61 on page 3D-136 (referred to, confusingly, as Table 6-3 in the text)). I am at a loss as to how to use the table to determine if the risk estimated for various scenarios are different from each other. I recognize the task is difficult and getting more so as the tools become more complex (e.g., the APEX, HDDM-CAMx, and Voronoi models). Nevertheless, quantitative uncertainty estimates can be estimated for most if not all steps in Table 3D-61 and IUA methods are available, and have been applied to support comments on past NAAQS reviews. See references provided in ISA comments.

I agree with the preference for the human exposure studies over the epidemiological studies in terms of having more confidence in their use. This stands in stark contrast to the approach used by EPA in the PM PA. As I stated in my comments on the ISA as it pertains to causality characterization, "quality human and animal experimental studies at relevant exposures need to be weighted over suggestive epidemiological (associational) studies to establish causality."

Questions from Dr. Masuca

Questions 1: The science on stratospheric tropospheric exchange of ozone is well known and discussed briefly in section 2.5.1.1 on page 2-27. While it can lead to a general increase in background ozone, the question is whether and how much it contributes to ozone NAAQS exceedances. The magnitude, frequency, and timing of such events become important. The effect is more pronounced and observable in high elevation western monitors. Much of this is discussed reasonably well in the rest of section 3.5. Since exceptional events are excluded from the risk analysis, it seems there should be more discussion of the exceptional events policy and the difficulty in making such demonstrations to EPA.

Question 2: All of the networks mentioned, including the road-side monitors provide important data for model performance evaluation and development. The road-side monitors should be mentioned in this regard. I would note that the 3 summer months operating schedule for PAMS sites needs to be re-

evaluated. Peak ozone is occurring outside these three months more frequently and data on other seasons is needed.

Question 3: I am assuming you are referring to what is used in the health studies. Although other exposure periods have been used, the human exposure studies summarized in the PA use 6.6 hour exposures. The epidemiological studies have used a variety of averaging time from 1 hour to annual average, including a max daily 8 hour.

Question 4: The diurnal patterns are driven by the relative magnitude of production and loss processes and the relative magnitude is variable across urban, rural, coastal, and elevation locations and time of day. Production is influenced by sunlight, temperature, humidity, etc. Losses include deposition (enhanced under a nocturnal boundary layer) and destruction through fresh NO emissions. While not comprehensive, this section describes the issue adequately.

Question 5: There is always locally generated and transported ozone from various distances. As mentioned above, the issue is how much background ozone contributes to ozone NAAQS exceedances. The magnitude, frequency, and timing of such events become important. The effect is more pronounced and observable in high elevation western monitors.

US background ozone is a term of art and, as such, is virtually impossible to measure. Even sophisticated monitoring using filtering is problematic from a source oriented point of view (see discussion on page 2-33). Models are uncertain but do track specific sources making them more amenable to a definition of what is included and excluded from US background and can do so for all locations. That said, which method is more accurate is not demonstrated in the document. An uncertainty analysis of the models is possible but explicitly excluded (see page 2-38). I find this paragraph completely inadequate, especially relying of a seasonal mean uncertainty of =/- 10 ppb when the risks estimates rely of hourly concentrations at specific locations. Uncertainty estimates need to be estimated in the context of the intended use of data or model results.

I believe the discussion on international emissions is reasonable and both anthropogenic and natural sources are discussed. All natural sources both foreign and domestic are included in USB. Only foreign anthropogenic are included. All US anthropogenic sources are the other side of the coin and this includes interstate transport (or other US state contributions to a given site).
The discussion of methane is warranted as it contributes to USB. As it is well mixed, its contribution is not very variable in space or time.

<u>Questions from Dr. Boylan</u>

Section 2.1: This section seem to be accurate and complete.

Section 2.2: See comments on same subject on ISA.

Section 2.3: See my response to Dr. Masuca's question 2 above.

Section 2.4: See my response to Dr. Masuca's question 4 above.

Section 2.5: See my response to Dr. Masuca's question 5 above. In addition, I continue to be concerned that model performance evaluation is less than robust. See my comments on the PM PA. EPA uses the old justification that performance is in line with the published literature (see page 2-37). The purpose of model performance in the literature tends to be different than the context of regulatory development. I realize this ship has sailed but it is still bothersome. Maybe if we ever get serious in conducting a true IUA, air quality model performance could be conducted in the context of driving the risk assessment. For example, how likely is it that an estimated exposure to one day above the benchmark concentration would actually be exposed to 2 or 4 days, or the reverse, assuming the activity patterns for the population are perfect?

Section 3.4.1: I have several concerns with this section. On page 3-48, the criteria for selecting the 8 areas are vague and not quantified. What are "exposure variation" and "population exposure conditions?" How do the eight selected areas vary in these parameters? Both definition and a summary table are needed. There needs to be a concise, simple summary (with examples) on how the ozone concentrations for the micro-environments are derived (page 3-49). I searched and found more detail on page 3D-56. The modeling is quite complex and data intensive. The sheer number of scenarios to be calculated seems quite burdensome and begs the question how accurate these are. What are the uncertainties? Finally, it is not clear how the benchmark concentrations (from the human exposure studies) and dose response relationships (from the epidemiological studies) were derived. This should be included.

Section 3.4.2: Since this is not a national assessment, like the previous section, more information is needed to understand the "diversity" represented by the 8 areas (see page 3-56).

Section 3.4.3: The messages in this section is confusing. Contrast the statements on page 3-61 with the summary paragraph on page 3-62. The latter is consistent with the message regarding the just meeting the current standard on page 3-57. EPA should eliminate the modifiers (e.g., markedly) on page 3-61.

Section 3.4.4: See my comments above on the need for a more quantitative integrated uncertainty analysis. The first paragraph describes a qualitative approach but does not direct the reader to where the parameters are summarized. The discussion on page 3-65 implies the adjustments to just meet the various levels is more certain but this is not demonstrated. It needs to be. Similarly on page 3-66 the statement "expected to more realistically estimate activity-specific energy expenditure" needs to be demonstrated. Similarly the last paragraph on page 3-68.

Section 3.4.5: No comments.

Section 3C.2: This section is even more meager than what is in section 3.4.1 (see above) and needs to be expanded to more completely justify the areas chosen and characterize their "exposure variations" and "population exposure conditions."

Section 3C.3: Page 3C-22 states all monitors were used whether they met data completeness or not. The rationale is based on Appendix U allowing nonattainment designation based on a monitor not meeting data completeness. While I can understand the Appendix U decision, I am not sure it justifies the use of that site for these purposes (i.e., APEX modeling). It would help if the method for filling in missing data were described.

Sections 3C.4.1 & 3C.4.2: On page 3C-23 EPA states "Differences in predicted O3 concentrations between the CAMx-HDDM configuration described here and a standard CAMx v6.5 simulation with full treatment of aerosol-O3 interactions did not influence O3 predictions in the urban study areas examined in this assessment." This implies that the sensitivities of the version used in the analysis were also not influenced. First, what does not influenced mean? Identical concentrations in every place and hour or something less rigorous? Second, was a comparison made of the sensitivities derived from both models (I recognize the CAMx v6.5 was probably not run in HDDM mode)? If not, I am not sure I would agree with their implication. EPA should demonstrate that the sensitivities were unaffected by the lack of tracking aerosol and cloud processing on the ozone sensitivities.

EPA did not included agricultural NOx but did include agricultural ammonia (see page C3C-27). For an ozone assessment this seems odd. And yet Table 3C-4 shows an entry for agricultural fire NOx but nothing for agricultural soil NOx. An explanation is needed.

Again model performance evaluation is not very robust and is much to aggregated. The data used in the risk assessment (the APEX model) is hour and location specific. Only regional/seasonal statistics are presented. How well does thee model do in a specific study area, at individual monitors, across gradients in a given hour or day? Model performance in the context of its use is needed. How does the performance affect exposure estimates?

Statements such as "reasonably captured general patterns of O3 transport within the northern Hemisphere" (page 3C-28) and "generally reproduce patterns of observed O3" (see page 3C-29) are subjective and should be backed up with quantitative information.

Section 3C.5: No comments.

Section 3C.6: Why was Voronoi Neighbor Averaging chosen over other methods? A rationale should be given and its uncertainty quantified.

Section 3C.7: No comments.

<u>Questions from Dr. Lange</u>

Question 1: While there may be exceptions, I would expect any changes in the annual averages to be small and could go in either direction. One question I would ask is what the epidemiological studies do when the monitors do not operate for the full year, which is the case of most monitors.

Question 2: I am not a statistician but I do not see how it could "protect against" confounding etc. Confounding exists or it doesn't. If one tests for confounding then maybe the higher statistical power allows it to be demonstrated more reliably.

Question 3: Yes, I believe those statements to be correct. I believe the statements are generally true and the caveat should apply generally, not to just ozone. I suspect the reason it is highlighted here in the ozone proceeding is because ozone concentrations may be more variable than, say, PM among micro-environments. Exposure is very dependent on the integrated levels of ozone in those micro-

environments, thus the use of the highly complex and data intensive APEX model. That said, it is not clear that why similar efforts are not done for PM and the other NAAQS. Studies have shown differences in PM and their species between the ambient and homes, restaurants, groceries, etc. In many cases PM is higher indoors due to numerous sources (e.g., cooking, dust, pet dander). Note that indoor sources of ozone (e.g., air purifiers) were explicitly excluded in this assessment. I find it curious that EPA expends so much effort with APEX on ozone and not PM. Finally, the whole APEX discussion implies but does not demonstrate that the complexities added to APEX result in a more accurate exposure estimate.

Questions 4 & 5: I do not have the expertise to address these questions.

Dr. Frederick Lipfert, Independent Consultant

General Comments

Most of my concerns involve human health effects, definitions of exposures, and the form of the NAAQS (averaging time). Some of them arise from recent literature; see below for example. Others relate to the failure of the O_3 ISA to consider all of the relevant epidemiology studies, notably those of my own and colleagues, listed in the Appendix. I regard premature mortality as the most important health endpoint because of its high assigned monetary values, its role in cost-benefit analyses, and the focus on the primary standard (Chapter 3).

That discussion focuses on respiratory effects, primarily morbidity, and delegates the more common and serious cardiovascular effects to a footnote. Shapes of dose-response functions and thresholds are not mentioned nor are residual risks at exposures below 70 ppb. I regard the most important exposure issue as that of indoor air quality and personal exposures, which are much lower than 70 ppb. The PA considers indoor exposures in great detail but they are ignored in the epidemiology. I find Chapter 3 to be inadequate.

A new long-term study of hospital admissions by Yazdi et al. (2019) deserves consideration. They created Medicare cohorts of admissions for stroke, heart attacks, and pneumonia and plotted exposure-response functions (ERFs) for annual average O_3 and $PM_{2.5}$ This is one of very few studies to consider long-term rather than daily hospitalization rates and to use annual average ozone rather than 8-h max. Ozone was statistically significant for all 3 outcomes. I extrapolated the ERFs and found ozone thresholds from 21-28 ppb. The extrapolated $PM_{2.5}$ ERFs showed a threshold of 4.5 µg/m3 for pneumonia admissions but residual risks for stroke and heart attack admissions. These results demand that ozone epidemiology be further considered as well as the form of the NAAQS. Below I list some relevant papers based on annual average ozone levels.

Questions remain about potential mechanisms for long-term health effects of ozone. Ozone is a powerful irritant to the respiratory system, but can it also initiate new cases of disease as hypothesized for PM? It is reasonable to expect cumulative vegetation damage from repeated exposures to O_3, lacking a repair mechanism between episodes, but some human respiratory effects are reversible. Given seasonal variability and the strong adsorption of ozone on indoor surfaces, it is hard to identify health effect mechanisms other than acute responses. Purported long-term effects may thus comprise the sums of short-term effects over the periods in question. None of the four new long-term studies listed below include the terms “cumulative” or “repeated exposure”, for example. Also, it is difficult if not impossible to conduct sufficiently long-term animal or human clinical testing that could support the long-term epidemiology.

Comments on the bulleted items in PA Section 3.6, "Key Uncertainties"

l. *Emphasis on at-risk populations in moderate exercise.* It would not be possible to clinically test the most susceptible individuals to improve the general understanding of the exposure- response relationship (ERF). The most important uncertainties in clinical

experiments are selection of subjects, the shape of the ERF, the importance of ambient temperature in this regard, the roles of co- pollutants.

2. *Exposures in epidemiology.* Consideration of indoor-outdoor exposure relationships in epidemiology is perhaps the most important issue, followed by timing of exposures including frequencies, latency, cumulative effects, and repeated exposures. In the absence of personal exposure information, ambient air quality must be considered as descriptive of the places where it is monitored rather than the exposures of inhabitants. Other examples of such descriptives include green spaces and traffic density, which was a highly significant predictor of mortality in the Veterans Cohort (see Appendix references).
3. *Different population groups.* Frailty of those at risk should be considered. Specific cohorts may be selected but would have limited applicability. Populations should be studied by age group.
4. *Co-pollutants.* Ozone never exists in isolation; co-pollutant effects must be considered with different exposure models, including indoors and time scales.
5. *Other photochemical oxidants.* The first consideration must be distribution in the atmosphere, thus requiring ambient monitoring. Clinical testing could then indicate which species are both hazardous and prevalent. My personal opinion is that improving our knowledge of ozone should take precedence over new species having poorly defined properties.
6. *Epidemiology with co-pollutants and temperature.* Temperature, ozone, and other pollutants such as PM comprise a 3-way system. Outdoors, ambient temperature strongly affects ozone formation but not PM, and all 3 may affect health over various time scales. Ozone is always reduced indoors, residential air conditioning (RAC) reduces temperature effects, but PM concentrations from indoor sources will increase when the house is closed up. The importance of RAC invokes socioeconomic factors in epidemiology.
7. *Ambient and indoor exposure considerations.* Spatial heterogeneity is a source of exposure error but indoor/outdoor differences are much more important. The likelihood of peak ozone levels in suburban or rural areas may require ambient monitoring networks denser than those now in place. Indoor ozone levels may only ~30% of outdoors.
8. *Exposure timing.* Short-term effects, especially mortality, must be summed over lag periods up to a week. Longer term exposures such as annual include the short-term effects experienced over the same period. More information, such as from clinical testing, is needed to understand repeated exposures, especially the timing between peaks.

9, 10. Personal exposure by season; activity levels. Time-activity levels must first be considered in epidemiology before those data could be used in predicting subsequent health effects including benefits from abatement. Clinical ERF data can be used for morbidity such as respiratory effects but not for mortality or hospital admissions.

<u>Recent epidemiology papers using annual average ozone concentrations</u>.

Lim CC, Hayes RB, Ahn J et al. Long-Term Exposure to Ozone and Cause-Specific Mortality Risk in the United States. Am J Respir Crit Care Med. 2019 200(8):1022-1031.

Danesh Yazdi M, Wang Y, Di Q etal. Long-term exposure to PM(2.5) and ozone and hospital admissions of Medicare participants in the Southeast USA. Environ Int. 2019 ep;130:104879.

Rhee J, Dominici F, Zanobetti A et al. Impact of Long-Term Exposures to Ambient PM(2.5) and Ozone on ARDS Risk for Older Adults in the United States. Chest. 2019 Jul;156(1):71-79.

Hernandez AM, Gimeno Ruiz de Porras D, Marko D, Whitworth KW. The Association Between PM2.5 and Ozone and the Prevalence of Diabetes Mellitus in the United States, 2002 to 2008. J Occup Environ Med. 2018 Jul;60(7):594-602.

Questions from Dr. James Boylan

Chapter 2 – Air Quality

- *Is the discussion on O_3 and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate and complete? If not, what additional information needs to be included?*

  Yes, it's adequate for this purpose.

- *Is the discussion on Sources and Emissions of O_3 Precursors (Section 2.2) accurate and complete? If not, what additional information needs to be included?*

  Yes.

- *Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3) accurate and complete? If not, what additional information needs to be included?*

  No. Indoor air quality information should be added.

- *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what additional information needs to be included?*

  Urban-suburban-rural concentration profiles for various averaging times would be of interest.

- *Is the discussion on Background O_3 (Section 2.5) accurate and complete? If not, what additional information needs to be included?*

  It would be useful to have historical trend data on background levels.

Chapter 3 – Review of the Primary Standard

- *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section 3.4.1) accurate and complete? If not, what additional information needs to be included?*

  I would like to see comparisons of risks by O_3 averaging times (annual, 24-h, 8-h, daily max) by season and health endpoint.

- *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard (Section 3.4.2) accurate and complete? If not, what additional information needs to be included?*

  Indoor infiltration and attenuation should be included.
- *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be included?*

  Personal exposures by age group.

- *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what additional information needs to be included?*

  No. See the discussion of Section 3.6 above.

- *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not, what additional information needs to be included?*

  This section should include considerations of health risks at background ozone levels for various averaging times.

Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses

- *Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Air Quality Adjustment to Meet Current and Alternative Air Quality Scenarios (Section 3C.5) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Interpolation of Adjusted Air Quality using Voronoi Neighbor Averaging (Section 3C.6) accurate and complete? If not, what additional information needs to be included?*

- *Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not, what additional information needs to be included?*

  I have no comments on this Appendix.

Questions from Dr. Sabine Lange

Air Quality

1) *Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time, over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are your thoughts about the change of annual average ozone concentrations (which tend to be the focus of epidemiology studies) with decreases in annual peak ozone concentrations?*

   I used the data for two frequency distributions from Figure 1 to estimate how cumulative risks could depend on the exposure-response function (ERF) threshold. I postulated a linear ERF so that the contribution to the total risk is the product of the frequency and the midpoint of the O_3 concentration bin (Figure 2). With no threshold or up to about 30 ppb, there is no difference in cumulative risk, as is the case with high thresholds (> 80 ppb). In the mid-range (thresholds from 40-80 ppb), the cumulative risk for the higher design value (DV) distribution is about double that of the lower one while the ratio of the 2 DVs is only 1.3, showing the importance of thresholds. Most epi studies have used some measure of peak O_3 rather than the annual average. My own studies (see Appendix) have used the 95^{th} percentile of the daily O_3 averages.

Epidemiology

2) *Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?*

   No; sample size only affects random error. Effects of measurement error, incomplete control of confounders, or a miss-specified model are independent of sample size. Cohort analyses are widely regarded as the best approach to studying long-term effects, but cohort sample size can only be increased by recruiting more subjects or extending follow-up time, which entails aging and loss of the more susceptible subjects.

3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40 and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to*

ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?

Yes, this is correct in all cases. Epidemiology deals only in numbers, not rationales. Reduced lung function may lead to hospitalization and then to death, but individual longitudinal analyses would be required to follow such a path. Each of these processes would require its own long-term analysis with its own confounders to be controlled and it is possible, perhaps likely, that different pollutants could be involved in each process (except for smoking). I know of no epidemiology studies that link sequential long-term effects. The time-series model of Murray and colleagues (see Appendix) postulates a frail subpopulation from which all daily deaths emanate in response to spikes in air pollution and/or temperature. An advanced version of this model solves for prior relationships with air pollution or temperature but the corresponding time scales are uncertain. This model decouples the causes of frailty from the causes of daily mortality which are likely to differ. Studies of daily mortality and hospital admissions have indicated similar relationships with ozone, but longer-term studies have not.

Exposure-Response Modeling

4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?*

I'm not aware of any "standard methods" for dealing with thresholds, aside from controlled (clinical) experiments that are sensitive to selection of subjects. A linear relationship may be the default option with noisy data for which the lowest concentrations may be the least reliable. However, there are good reasons to accept the concept of (essentially) zero threshold, that differ between long- and short-term analyses. The time-series model of Murray and colleagues analyzes daily mortality relationships in terms of the combination of subject frailty and air pollution. Death may result from excess frailty or excess pollution or both. As a result, in a sufficiently large population there will likely always be someone sick enough to succumb to a small air pollution perturbation; the threshold depends on the population at risk. The situation with long-term effects is more complicated. They result from cumulative or repeated exposures after a period of latency, so that effects of pollution abatement will be delayed and it becomes difficult to define the appropriate exposure over the periods involved. Background ozone will also play a role. Here the threshold depends on the characteristics of exposure. Finally, health responses during a year will be the result of both long-and short-term exposures, so that even in the absence of long-term effects there may be pollution-related mortality at any outdoor concentration level. Also, different pollutants may be involved at different time scales.

5) *The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?*

Most epidemiology studies assume a homogeneous population at risk which may be convenient but is unrealistic. The remaining life expectancies of those aged 65 and over range from one day to 35 y or more with a median around 15 y. (This situation pertains for populations but not necessarily cohorts, depending on subject selection.) Many air pollution epidemiology studies have shown higher risks for subjects with pre-existing conditions. Lung cancer mortality rates are proportional to the cumulative cigarettes smoked, even though not all smokers get lung cancer. Following this model, we would expect air pollution-related mortality to respond to cumulative exposures from a few days to decades, depending on many other variables including preexisting disease. The answer to this question is thus: Yes, air pollution epidemiology includes all degrees of susceptibility but the most highly susceptible subjects may dominate the group response.

Questions from Dr. Corey Masuca

1) **2.1. Ozone and Photochemical Oxidants in the Atmosphere**

How sound science is this mechanism of ozone transfer between the stratosphere and the troposphere?

I don't see this as relevant to the setting of NAAQS levels.

2) **2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks**

While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET, National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road Monitoring Sites, especially for NOy?

I'm not familiar with these networks.

3) **2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards Are Met**

There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is this short-term 8-hour rolling average consistent with short-term actual and scientific studies?

I believe so.

4) 2.4.3 Diurnal Patterns

While this section refers diurnal patterns of relative ozone concentrations between day and night, are these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant weather conditions? What about the effects on topography/geography in determining diurnal patterns?

> It's my understanding that the mechanism is controlled by UV light and that temperature accelerates the reactions. To sort out these interactions, I would like to see clinical health effect experiments using ozone exposures at various temperature levels. Los Angeles and the Utah Valley offer examples of topographic influences on ozone photochemistry.

5) Background Ozone

There, in general appears to be a lot of discussion about background ozone concentrations from transport and natural sources. However, are most salient ozone concentrations more localized and from anthropogenic sources?

> This depends on what is meant by "salient" and may depend on contributions of other photochemical oxidants.

This section references the utilization of photochemical grid models due to the lack of ability to characterize the origins of ozone and the ability to estimate the magnitude of background ozone. However, how predictable are these photochemical models, especially given the highly photolytic and relative instability of ozone in the atmosphere?

> This is a question for the modelers. Relevant questions concern indoor, outdoor, and background temporal patterns and diurnal cycles.

This section mentions that international emissions sources via transport mostly originate from anthropogenic sources. However, is there a possibility that there can be international transports from non-anthropogenic/biogenic sources?

> I suppose so.

Also, this section noticeably leaves out non-international, interstate transport of ozone.

> Interstate transport should be accounted for by the usual photochemical grid models that don't recognize political boundaries.

6) 2.5.1.6 Pre-Industrial Methane

There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance of methane with respect to the formation of and consideration of ozone? Is a discussion on methane warranted?

I don't think so. It's up to the PA to provide linkage.

Relevant Publications by Lipfert and Colleagues Not Cited in ISAs or PAs

Daily Mortality Publications

Murray CJ, Lipfert FW. Revisiting a Population-Dynamic Model of Air Pollution and Daily Mortality of the Elderly Population in Philadelphia. J Air Waste Manag Assoc. 2010 60:611-629.

Murray CJ, Lipfert FW. A new time-series methodology for estimating relationships between elderly frailty, remaining life expectancy, and ambient air quality. Inhalation Toxicology 2012 24:89-98.

Lipfert FW, Murray CJ. Air pollution and daily mortality: A new approach to an old problem. Atmos Environ 55; 467-74 (2012).

Murray CJ, Lipfert FW. Inferring frail life expectancies in Chicago from daily fluctuations in elderly mortality. Inhal Toxicol. 2013 Jul;25(8):461-79.

Long-term Cohort Mortality Publications

Lipfert FW, Perry, H.M. Jr., Miller, J.P., Baty, J.D., Wyzga, R.E., Carmody, S.E. (2000) The Washington University-EPRI Veterans' Cohort Mortality Study: Preliminary Results, Inhalation Toxicology 12 (Suppl 4):41-73.

Lipfert FW, Perry, H.M. Jr., Miller, J.P., et al., 2003. Air Pollution, Blood Pressure, and Their Long-Term Associations with Mortality. Inhalation Toxicology 15, 493-512.

Lipfert FW, Wyzga, R.E., Baty, J.D., Miller, J.P., 2006a. Traffic Density as a Surrogate Measure of Environmental Exposures in Studies of Air Pollution Health Effects: Long-term Mortality in a Cohort of U.S. Veterans, Atmospheric Environment 40, 154-169.

Lipfert FW, Wyzga, R.E., Baty, J.D., Miller, J.P., 2006b. $PM_{2.5}$ Constituents and Related Air Quality Variables as Predictors of Survival in a Cohort of U.S. Military Veterans, Inhalation Toxicology 18:645-57.

Lipfert FW, R.E. Wyzga, Jack D. Baty, J. Philip Miller. Vehicular Traffic Effects on Survival within the Washington University - EPRI Veterans Cohort: New Estimates and Sensitivity Studies, Inhalation Toxicology 20:949-960 (2008).

Lipfert FW, R.E. Wyzga. On Exposure and Response Relationships for Health Effects Associated with Exposure to Vehicular Traffic. J Expos Sci Environ Epidem 18: 588-599 (2008).

Lipfert FW, Wyzga RE, Baty JD, Miller JP. Air pollution and survival within the Washington University-EPRI Veterans Cohort: risks based on modeled estimates of ambient levels of hazardous and criteria air pollutants. J Air Waste Manag Assoc. 2009 59:473-89.

Lipfert FW, Wyzga RE. Revisiting the Veterans Cohort Mortality Study: New results and synthesis. J Air Waste Manag Assoc. 2018 Nov;68(11):1248-1268.

Lipfert FW, Wyzga RE. Environmental Predictors of Survival in a Cohort of U.S. Military Veterans: A Multi-level Spatio-temporal Analysis Stratified by Race. Envir Res (in press 2019)**.**

Dr. D. Warner North, NorthWorks

My comments on the draft Policy Assessment follow themes from my earlier comments on the draft PM Policy Assessment and the draft Ozone Integrated Science Assessment. I remain concerned about confounding in the interpretation of epidemiological data. I believe modeling of exposure level to health response needs to be done carefully, reflecting biological knowledge and expert judgment. I have substantial concerns about how EPA has modeled both air quality and exercise patterns to predict the health responses that were termed adverse in revising ozone standard in 2015. I remain concerned about wildfires as an important source of ozone exposure at unhealthy levels. Wildfire plumes may have contributed to Sacramento, California being the highest in ozone levels of the eight metropolitan areas that EPA used in its PA analysis.

While the draft PA represents a great deal of work in assembling information, it is disappointing that there is so little new information on human clinical studies or in assessing impacts on asthmatics, as might be measured by hospital admissions or emergency department visits in areas with high ozone levels.

Although I am not trained as a medical professional I have extensive personal experience with the frequency and severity of asthma episodes. The most common triggers for a bronchospasm ("asthma attack") come from pet dander, dust mites, and cockroaches, not air pollution. (https://www.xolair.com/allergic-asthma/what-is-allergic-asthma/allergic-asthma-triggers.html). These common triggers may be more frequent in low socioeconomic status locations. Asthma patients control their airway reactivity with inhalers such as albuterol, and for more severe cases, corticosteroids. These medications may be needed frequently (several times per week, or even daily). Especially for severe asthmatics, activities involving exercise may be moderately to severely curtailed. Yes, air pollution can trigger or aggravate asthma. (https://www.asthma.com/what-is-asthma.html). But the context ought to be considered – for most asthmatics, air pollution at, or near, present standards is a minor contributor to their symptoms and their need for medication. Most asthmatics are not going to do prolonged exercise out of doors, especially on days with an unhealthy air warning. As one who has personal experience over decades with a severely asthmatic patient and also with an adult with cystic fibrosis, I am skeptical about the analysis used in 2014-5 for the previous round of ozone review. The distinction between responses at 60, 70, and 80 ppb exposures is based on only a few studies, most of them not recent. Inflammation is not well defined and measured. Virtually all observed symptoms including lung function decrements (FEV1) and airway reactivity are transient, going away after a few hours to a day. But: exposure to unhealthy air in the form of a wildfire smoke plume persisting over a metropolitan area for many days should be viewed as a serious public health threat to people such as the two I am close to. Exposure or potential exposure to smoke plumes this year and last year have motivated decisions about getting masks, special filters for air conditioning systems, and sending the sensitive person(s) out of the affected area until the air clears.

Nearly four decades ago, at a time when I was first involved in working on air pollution health effects, there were repeated episodes in a European city of asthma attacks in which many people went to hospital emergency departments for treatment. The incident was initially blamed on air pollution from an electric power plant. More careful investigation indicated it came from unloading ships in the harbor, and the main culprit was soybean dust. The reference is Antó et al., *New England Journal of Medicine*,

1989. Yes, air pollution can trigger episodes of asthma attacks across an urban area. But indoor air pollution from pets, dust mites, and cockroaches is much more likely to be the trigger for asthma attacks in urban areas of the United States.

The studies listed in Appendix 3B on emergency department visits (EDV) and hospital admissions for asthma include numerous ones on New York City and Atlanta, Georgia. I found only one, state-wide study for California, Malig et al., 2016, with data from 2005-2008. This study showed a small increase (1.5 to 3.9% per 10 ppb O_3) for EDV for asthma and upper respiratory infections using warm season data. (Full year results were slightly smaller.) A little less than half of the EDVs were for children 18 and under, rather than adults. I would characterize these results as weak association evidence motivating further studies. The authors' final sentence is, "Studies examining the health benefits of ozone reductions should try to account for ozone-EDV relationships to get a fuller picture of those benefits." I heartily concur.

Questions from Dr. Corey Masuca

1. I do not have a background in the specifics, but I believe the mechanism has been well established in the scientific literature for many decades. Here is a reference to an article by a Norwegian scientist from 1960: Storebø, Per B., "The exchange of air between stratosphere and troposphere," Journal of Meteorology 17:547-554 (1960). During the 1960s there was much interest in the radioactive isotopes from nuclear testing coming from the stratosphere into the troposphere. There are many other papers you could find with a search on the web.

2. Near Road Monitoring sites are most important for determining how ozone and precursors change between emissions on a road or highway and ozone levels at locations a short distance away. The ambient air monitoring discussed in this section and Section 3 is at the regional and national scale, rather than the local scale. I note for your attention my responses to Dr. James Boylan regarding Section 3 and Appendix 3C. The calculations made by EPA for its Section 3 analysis were done with a national model, CAMx, with a 12 km by 12 km grid. That is the size of the City of San Francisco, 50 square miles! Local peaks and valleys in ozone levels are not predicted with a model of this large grid size. There are comparisons in 3C.4.2 of model predictions at the grid cell level and monitoring station(s) within the grid cells. The figures in this subsection show the relatively large differences between the model predictions and MDA8 observations. Only one year of data is used for the model predictions. I believe use of a model with a much finer grid size would be useful for areas violating the present standard, and data from ***all*** the available monitoring stations should be collected and used. It would be important to examine multiple episodes over many years of prolonged high ozone levels, not just one year, to determine the mix of ozone created out of the local area with ozone from local and nearby NOx and VOC sources. I did not find evidence in Section 3 and Appendix C that EPA has done such local analysis or emphasized prolonged high ozone episodes from multiple years. Section 3C.6 describes a mathematical system ("Voronoi Neighbor Averaging") for scaling the CAMx predictions at the monitoring sites to census tract centroids, and these interpolated predictions of ambient ozone levels are used to predict the incidence of health effects for the people in the census tract. (See page 3C-91 for an illustrative diagram. See Figures3D-2 to 3D-5 for pictures of the census tracts.) Local chemistry of ozone formation and absorption on a scale of less than about 10 miles cannot be done with this EPA modeling system. Ozone peaks produced by, for example, rush hour traffic concentrations in an urban

area cannot be examined: the "grain size" of EPA's analysis is too big! Compare to the data in Figure 2-5, page 2-12. In the 2015-2017 data the exceedances of the MDA8 70 ppb are appearing only in one broad region, California's Central Valley plus Los Angeles to San Diego (coastal urban areas with mountains to the east creating a "mountain bowl"; the Central Valley is a big "mountain bowl") -- and in a small number of urban areas – Phoenix, Seattle, Salt Lake City, Denver, Dallas, Houston, Chicago, and the Boston- Washington corridor. It would be useful to have analysis that focuses on these (non-California) urban areas in finer detail. My concern for the California region is that wildfires may play a critical role in causing a large fraction of the red and orange circles in Figure 2-5, which are exceedances of the current 4th worst 8-hour-average day-in-a-three-year-period (MDA8) standard. We should know more about the exceedances in the urban areas other than in California, which are not due to wildfires but to other sources of NOx and VOCs.

3. I am not expert on the details, but I think there is a well-defined protocol for computing the maximum 8-hour average from hourly concentrations. I believe it is described in one of the Appendices, probably in the ISA if not the PA, but in my available time I did not find a page reference to give you.

4. Sunlight drives the photochemical formation and destruction processes for ozone, so what is being discussed in section 2.4.3 is primarily related to the presence/absence of sunlight, that is, day versus night. The length of the day enters as seasonal variation. Temperature and topography/geographical factors affecting air movement are all important for understanding the processes for formation and destruction of ozone. This complexity should be included in the modeling. As I have described under 2, EPA's system cannot accommodate local detail.

5. My big concern on 2.5.1.3, including wildfires as part of Background, "USB." I think wildfires as well as prescribed fires should be considered as anthropogenic sources and not as background. Wildland fires can lead to levels of both $PM_{2.5}$ and ozone far above current standards. At least in this PA "wildland fires" get called out for a heading in the *Table of Contents* and two paragraphs that make it clear that wildfires fires can be an important contributor to ozone exposure in regions where these fires occur. The high exposures from large wildfires should not be kept out of sight by deleting them from the data as "exceptional exceedance" events. They should be considered as the consequence of human activity – in particular, national, state, and local policies that influence the occurrence and severity of wildfires. The adverse health effects are quite real to those who suffer them. Whether or not a state gets relief from whether these "exceptional exceedances" trigger a finding of non-compliance with a NAAQS may be important because of penalties for non-compliance. That is a separate matter from protecting public health.

6. Methane can be the VOC that forms ozone in the presence of NOx and sunlight. Usually other VOCs are more important, but if these others are not present then methane contributes to NOx formation. The ISA had extensive discussion on the role of methane. Yes, in is true that in our post-industrial society we have a lot of sources of methane such that there is much more than in pre-industrial times, and we are uncertain on how much more methane we now have. But that uncertainty will be much more important for climate alteration from CH4 as a greenhouse gas than for methane contributing to peak levels of ozone above the primary standard. I would say that extensive discussion should be in the ISA rather than the Policy Assessment, since controlling sources of methane is not a focus for the Policy Assessment document now under review. I do not find the three-paragraph discussion in 2.5.1.6 as inappropriate as I do the huge amount of complex detail elsewhere in this long document.

Questions from Dr. James Boylan

Overall, for the three portions of the PA that you chose to ask about, your question of whether it is accurate and complete has led me to comment on what I think about the whole PA draft document, which I have done in my earlier general comments. By and large, I think EPA staff have worked hard and done a good job in assembling a great deal of relevant material. I don't think any document of this type can ever be judged as complete. I think a major goal of the document should be to focus attention on research needs as well as policy needs. The document should be an evolving guide to both government officials and interested parties on the public. Trying to make it more "complete" might add much more detail that is superfluous to the interests of most readers. It should be accurate in the sense that it does not mislead readers. The material on inflammation at low exposure levels in the ISA draft is, in my judgment, at least borderline misleading in suggesting evidence for inflammation at levels at or below the standard. As I expressed in my ISA comments, I thought the support for these statements in the ISA was weak. The discussion in the PA seems a bit better in citing what was actually written by authors of the studies. Section 3.5, page 3-74 line 29-232 cites the ISA rather than the preceding portions of the PA. I repeat my objection to the words, "respiratory inflammation" in this sentence as inaccurate as stated, without any caveats. Two sentences on page 3-76, lines 9-14, are slightly better, indicating that "inflammatory response and airway responsiveness" are "reported for higher exposure concentrations" rather than at "concentrations slightly above 70 ppb with intermittent exercise." See also footnote 69, page 3-76.

Air Quality: Chapter 2. I am a risk person with a physics background, so I can review this chapter with a modest level of understanding but not a close familiarity with recent literature. I find the chapter generally good and have only one major criticism, which is a policy dissent with EPA that I have raised in my previous two response submissions. I do not think wildfires should be considered as background, but as anthropogenic sources that can be strongly influenced by strategies on management over land areas where wildfires occur.

Chapter 3: Review of the Primary Standard. You focus your questions not on this whole chapter, but on Sections 3.4.1 to 3.4.5, page 3-45 to 3-72, 28 pages. You do not include section 3.5, the evaluation of the available evidence as of 2019 and the recommendation that the primary standard, lowered in 2015 from MDA8 75 ppb to 70 ppb, be maintained, or the discussion of the Administrator's reasoning in revising the standard from MDA8 75 ppb to 70 ppb, described in Section 3.1.1.

There is relatively little that is new in the 28 pages. Almost all of it is very similar to what was provided in the EPA Health Risk and Exposure Assessment (HREA) in 2014. Is the reasoning used by the Administrator (after advice from CASAC and the public) valid today? Is there important new information? Might the standard be viewed as overprotective, compared to the previous standard of 75 ppb? Or is it in need of further tightening? Children including asthmatic ones in the Sacramento area experience MDA8 exposure well over the 75 ppb level. How much of public health problem does this pose? Asthmatics and children in other urban areas are experiencing levels in the high 60 ppb range and above. Is their health being protected with an adequate margin of safety? What strikes me as odd is that there is so little described in Section 3.5 beyond the reasoning of a previous Administrator described in Section 3.1.

You asked about Appendix 3C, which presents a great deal of information on population exposure. Appendices 3C and 3D support the Section 3.4 modeling exercise on how many health effects might be expected with reductions in ozone precursors such that the eight metropolitan areas just meet a MDA8 standard, with calculations for 75, 70, and 65 ppb. The Appendix 3C material is extremely detailed, and it does not tell us about the extent of observed or predicted public health effects under current levels of ozone exposure, as opposed to these projected "design values" to just meet a standard.

Here are some brief notes on Sections 3C.2 to 3C.7. In Section 3C.2 EPA describes the eight study areas. The section does not explain in any detail why these eight were selected – seven are holdovers from 2015. The extent of the explanation is one sentence, lines 8 to 10 on page 3C-13. Section 3C.3, Ambient Air Ozone Monitoring Data, describes the procedure for determining the NOx emissions changes needed to meet the three MDA8 standards. The maps show us the location of monitors, including buffer sites used for interpolation for modeling air quality. Section 3C.4.1 tells readers that the CAMx model was used with the Higher Order Direct Decoupled Method (HDDM). The CAMx model covers the lower 48 states and adjacent areas of Canada and Mexico with a 12 by 12 kilometer grid, and it was run for all of 2016 including a startup period in late 2015. (This is one year of weather, with a grid cell size of 50 square miles. Local scale phenomena will not be captured in such a system.) Weather data for 2016 came from a mesoscale numerical weather prediction model, and 36 vertical layers are used for this and for CAMx. (Later in the 3C text 44 levels are indicated.) The alpha version of the Inventory Collaborative 2016 emissions was used. Emissions for wildfires and prescribed burns were included. (If any periods were deleted as exceptions, this is not noted, and ***any such exclusions of emissions should be disclosed***.) 3C.4.1.6 describes initial and lateral boundary conditions. Section 3C.4.2 discusses how well the CAMx model can reproduce the actual measured 2016 O_3 concentrations. We are told the predictions "generally reproduce patterns of observed O_3. The notable exception is a persistent underestimate in winter across almost all regions, particularly at the higher latitude sites." (page 3C-29, lines 2-4.) Then a large amount of statistical data and maps are given in support.

EPA has amassed a huge amount of detail on modeling ozone in ambient air nationally on a large grid. Details about local topography and sources such as concentrations of vehicular traffic and major stationary sources are absent. There is no calculation at this stage on what is in indoor air, as opposed to outdoor air. Does the smoke plume from a large nearby wildfire blow into a metropolitan area, or does the plume bypass the area? This depends on the wind direction. Data from only one year will not reveal patterns that may cause the peak ozone exposures over a period of three years, five years, or longer. For seasonal ozone averages over the lower 48 states I would expect a general match, but I doubt if peak ozone concentrations leading to MDA8 standard exceedances at individual monitors will be well reproduced. Figure 3C-13 to 16 indicate a normalized mean bias of the order of 20 ppb in the northeastern United States, with a larger discrepancy in winter. For concern about peak ozone levels in the Washington to Boston metropolitan corridor, that is not great accuracy. In the west with higher background, the validity of the model prediction may be even more questionable in terms of the frequency of exceedances above the standard at specific monitors. See Figures 3C-40 to 43.

Section 3C.5 discusses air quality adjustments, specifically, reductions in NOx emissions to just meet the standards. We are told that EPA used this approach for the 2015 O_3 NAAQS review. This is an effort (using a very detailed model of only moderate accuracy on a regional basis) to predict ozone levels if NOx reductions were made so as to allow the standards to be just met. The chemistry is non-linear, and so there is an HDDM adjustment process. In some metropolitan areas (e.g., Sacramento) big emissions

reductions will be needed to meet standards.) Then in 3C.6 we learn about interpolating from a 12 kilometer grid size to 500 meters and centroids of census tracts. How well does this work in downtown urban areas with street canyons? What is the variability of ozone readings within a few kilometers of a monitor?

In 3C.7 all of this is put together to compute results, design values for patterns of ozone exposure over the urban areas. Perhaps something can be learned from this exercise, but it should be realized that it is an effort to go from a lower 48 scale to predict on a "neighborhood" scale, with assumptions compounded all along the way.

My summary on the completeness and accuracy of 3C2 through 3C7 is as follows. Yes, EPA staff have told us what they have done, and it appears to be little changed from what was done in 2015 to calculate risk numbers for health effects under alternative standards. In several weeks of reading of documentation outside the PA and its Appendices, one might be able to find all the details on what was done. I did not have time or motivation for such investigation. I judge the accuracy of the predictions to be very limited, especially for calculating peaks, the fourth highest 8 hour average over a three year period.

The collection of models and assumptions produces apparently precise numbers about how many health effects might occur under alternative standards. See the discussions supporting the choice of a 70 ppb standard in Section 3.1 and 3.5. The key uncertainties not covered in 3C are the assumptions about human behavior, exercise patterns, and exposures outdoors and indoors where the presence or absence of air conditioning may be important. (The methods are described in Appendix 3D.) I would like to see regional studies using local models, knowledge about socioeconomic status by neighborhoods and involvement of state and local air pollution experts who might know about "hot spots" of peak exposure, and their proximity to schools, playgrounds, sports arenas, and other locations where children and adults might be exercising out of doors for the order of six to eight hours. And do the exposed people learn about unhealthy air conditions and change their behavior so as to avoid exercising at times of high ambient ozone levels? In the unhealthy air from recent wildfires in northern California, schools were closed and sporting events were cancelled. Does an asthmatic want to ride her bike to work on a unhealthy air day, or will she opt for using her car or public transportation?

Section 3.6 of the PA describes key uncertainties and areas for future research. There should be much more attention to "understanding of O3 effects" in the range of 70-120 ppb, and not at "below the lowest concentrations studied," which would mean below 60 ppb (page 3-88). Human behavior is hard to predict. Better understanding is needed on who is at high risk by exercising outdoors under high ambient ozone conditions. Sensitive subgroups such as children and asthmatics need to be protected. How great is the need for protecting them in areas and cities experiencing MDA8 exposures near and above 70 ppb, sometimes above 100 ppb, based on Figure 2-5, page 2-12?

What EPA staff did in examining eight metropolitan areas was to model ozone exposures under a set of assumptions that emissions reductions would occur such that these areas ***would just comply*** with the standards. Were the health impacts predicted at these computed-by-model with assumed patterns of human activity judged to be acceptable for protecting public health with an adequate margin of safety? Yes. that was the claimed goal for the analysis, to enable an evaluation of model predictions of health effects from model predictions of air quality. There is little evidence that EPA worked with its Regional

Offices, with state agencies, and the research community ***to ascertain the magnitude of the public health impacts of recorded actual ozone exposures*** in the most recent years, from 2015-2017 to the present, in areas where exposures exceed the standards by a large amount. Why not, as a supplement or a better use of EPA resources, go to Sacramento as the city with the highest ozone exposure (e.g., Figure 3C-81, page 3C-114; Figure 3C-103, page 3C-138) and learn more from the medical professionals in this metropolitan area about the extent to which asthmatic children in that area were suffering health exacerbation, such as inflammation, pain on inspiration, and increased airway responsiveness?
The numbers in Table 3.3 page 3-58 reflect that with air quality just meeting an MDA8 standard of 70 ppb, exposures at 80 ppb and even 70 ppb are quite rare, and exposures above 60 are relatively infrequent, an average of 3 to 9% for children with asthma and slightly less of all children experiencing one day per year of exposure while breathing "at an elevated rate." Compare Table 3-5, with air quality just meeting a higher MDA8 standard of 75 ppb. The numbers for affected children nearly double to about 7 to 16%, because exposures above 60 ppb are projected to increase by that much.

Sacramento is far from meeting a 75 ppb standard. In order ***to bring Sacramento into compliance with the present MDA8 70 ppb, a reduction of 58% in NOx precursor emissions is estimated to be needed.*** A 45% reduction would be needed to meet the old standard of 75 ppb. These are a big numbers! No others of the seven metropolitan areas would need more than a 23% reduction in emissions to meet the old standard of 75 ppb. IF the standard were reduced to 65 ppb, Sacramento would need a reduction of 72% and the need for the other seven areas would be in the range from 38 to 68%. The numbers are large for Sacramento because Sacramento has a high background ozone level, "USB," as EPA uses this term. Phoenix also has high background. Phoenix could meet the 75 ppb standard with an emissions reduction of 14%. But for the 70 ppb standard, Phoenix would need to reduce its emissions by 49%, approaching the high number for Sacramento. Some of that ozone comes from wildfires, now counted as background. Note in Figure 3C-103 the red squares in the observed data, above and below Sacramento in rural adjacent counties. These might have come from the large wildfire plume(s) in the year 2017. (Numbers in this paragraph come from Table 3C-19, page 3C-89.)

Critical commentaries on EPA's modeling. The PA and the ISA do not acknowledge published criticisms of the methodology used in 2014-15, and used again in this 2019 PA with only minor changes. I have not have the time to find more than a few examples of such criticism, but in reviewing three EPA draft documents I have found little evidence that EPA has included criticisms in peer-reviewed journals, presentations at EPA public meetings, and written comments from members of the public.

In my comments on the Ozone ISA I discussed the Belzer–Lewis paper recently published (2019) in *Risk Analysis*. I will not repeat these comments, which CASAC members should have in my earlier submission on the ISA. Another paper pointing out the uncertainty in estimating FEV1 decrements is Glasgow and Smith (2017). Modeling uncertainty on the concentration response relationship should be considered as well as statistical uncertainty. Neither of these papers is referenced or discussed in the ISA or PA. The Glasgow-Smith paper discusses the methodology used in EPA's Health Risk and Exposure Assessment (HREA) from 2014. Essentially the same methods appear to have been used in generating Table 3.3, based on the McConnell et al. papers from *Inhalation Toxicology*, 2012 and 2013. (See footnote 64, page 3-57, which explains that there are "a number of differences between the 2014 HREA and the quantitative modeling and analysis" in the PA, with these details discussed in Appendix 3D. The HREA and the two McDonnell et al. papers are referenced in the PA Section 3.

Another missing reference from Section 3 (and not in the Jaffe et al., 2018 reference in the PA) is the work on wildfire plume exposures by Larsen et al. (2017). Here is a quote from the *Science Digest* summary: "While plumes had occurred only on 6-7 percent of days, these plumes accounted for 16 percent of unhealthy days due to small particles and 27 percent of unhealthy days due to ozone." A direct quote from Larsen et al. follows: "Smoke-plume days accounted for a disproportionate number of days with elevated air quality index levels, indicating that moderate increases in regional air pollution due to large fires and long-distance transport of smoke can tip the air quality to unhealthy levels." (The data in Larsen et al. are from 2006-2013. The numbers could be much higher for 2017-2019, when Northern California has had large wildfires affecting air quality in the Central Valley (including Sacramento) and the San Francisco Bay area.)

Questions from Dr. Sabine Lange

1. I fully agree that the decrease in annual average ozone exposure is significant. I continue to have concerns on whether the epidemiological results imply manipulative causality as opposed to association, and I am pleased to read that EPA is not using these epidemiological results but rather basing its recommendations (for the last round and the present one) mainly on human clinical studies. There are still areas of the US, such as the Sacramento area, that have MDA8 levels well above the current standard of 70 ppb. I would like to see CASAC focus on the public health risk in these areas. See my general comments above regarding asthma. There ought to be more research to see if high ozone episodes in Sacramento (and elsewhere in the Central Valley and the Los Angeles to San Diego area) have led to increases in hospital admissions and emergency department visits.
2. No. I responded to a similar question in the O_3 ISA. Statistical power comes from having a large sample size, and NOT from having resolved issues of confounding, error, and bias. Consider we have a study of 10 million children showing that shoe size predicts reading ability. Because data were obtained from 10 million children, a very large number, the confidence interval is quite narrow. Does this apparently accurate prediction imply that getting children larger shoes will improve their reading ability? No way!
3. I am inclined to think that the problem is a general one that will only be resolved by getting data on potential confounders such as income (more generally, socioeconomic status), and extremes of temperature, which have large impacts on mortality and morbidity via mechanisms independent of air pollutants. However, we should understand that at VERY high exposure levels, air pollutants such as ozone and fine particulate matter (e.g., smoke) can cause illness and death. The shape of the exposure-response relationship is critical for assessing the risks. Extrapolation over orders of magnitude is readily done with available mathematics. But how this extrapolation is done should reflect judgment on the biological mechanisms underlying damage to health.
4. Yes, assuming a lack of threshold has become a standard method in many areas of EPA's risk assessment practice. Many of us old-timers believe this practice is questionable, because absence of evidence is not evidence of absence. The biological mechanisms underlying the adverse health response should be assessed based on available information including judgment. Traditional toxicology has used a sigmoid shaped exposure-response function, on the basis that very small exposures (episodic or cumulative) are unlikely to trigger an adverse response but as the

exposure increases, the body's defenses and repair mechanisms can become inadequate, so the adverse effect becomes common in an exposed population. And the response may saturate with most or all of those who are susceptible to it having the adverse response – e.g., given enough bacteria in the spoiled food, nearly everyone gets sick from eating it. But linearity to zero became common in cancer risk assessment. This assumption was originated as a health-protective default assumption for screening: a plausible upper bound for identifying chemicals deserving more detailed risk analysis, and not for estimating the incidence of human cancer. But linear to zero is often used for the latter purpose.

5. I am concerned that FEV1 decrements are not a good indicator for adverse health impacts in sensitive populations. (See my general comments at the beginning of this response. FEV1 measurements vary a good deal. The Belzer-Lewis paper mentioned in my O3 ISA response has perceptive criticism about using FEV1 data in research.) It seems to me that lack of information, referring to the words you use in your first sentence, (1) should motivate detailed studies of the people that are judged to be at highest risk, and (2) leaders of agencies such as EPA should think beyond legally required standard setting to the bigger issue of how to protect public health with an adequate margin of safety. If adverse health effects are judged to be essentially absent for much of the United States (a reasonable inference from Figure ES-1 in the ISA and Figure 2-5, page 2-12 in the PA), then attention should be focused on the remaining areas where such adverse health effects may still be occurring. Are these adverse health impacts really there in these remaining areas, or are our government officials being overly precautionary and protective in setting standards, but ignoring major public health protection needs by assuming that some causes, such as wildfires, are "natural background?" ***EPA should be using common sense and not be trapped in traditions that violate common sense.*** The levels of ozone and fine particulate matters that millions of people in California have experienced from wildfire smoke plumes in 2017, 2018, and 2019 are far above the NAAQS standards and pose serious health effects, especially to members of sensitive subgroups. Some of these people are among my family, my friends, and my neighbors. The costs involved in reducing these risks to health from wildfire plumes are very large. So are the costs of bringing ozone levels in Sacramento into compliance with a 70 ppb MDA8 standard, even if with wildfire periods are exempted. (In my humble judgment, the former activity makes much more sense than the latter.) EPA staff and CASAC should acknowledge these facts in their written documents, as part of advising the EPA Administrator on strategy with respect to criteria air pollutants. I believe giving such advice is within the legal mandate of CASAC under the Clean Air Act.

   Comment: I appreciate and endorse the message in the graph you show in your questions for the St. Louis area comparing 2001 to 2003 with 2013 to 2015. Please consider also a graph of the same sort of data for the Sacramento area for 2017-2019, compared to earlier years with no big wildfires, such as 2013 to 2015. The message will be almost opposite. Compliance is not nearly achieved, but a distant and receding goal, especially if wildfires are not exempted.

References not in the PA

Garrett Glasgow and Anne E. Smith, "Uncertainty in the Estimated Risk of Lung Function Decrements Due to Ozone Exposure," *Journal of Exposure Science and Environmental Epidemiology* 27:535-538, 2017.

Alexandra E. Larsen, Brian J. Reich, Mark Ruminski, Ana G. Rappold, "Impacts of fire smoke plumes on regional air quality, 2006–2013." *Journal of Exposure Science & Environmental Epidemiology*, 2017; DOI: 10.1038/s41370-017-0013-x. Summary in *Science Daily*: https://www.sciencedaily.com/releases/2018/01/180109112415.htm.

J.M. Antó, J. Sunyer, R. Rodriguez-Roisin, M. Suarez-Cervera, and L. Vazquez, "Community outbreaks of asthma associated with inhalation of soybean dust," *New England Journal of Medicine*, 320(17):1097-1102, 1989.

Questions from Dr. James Boylan

Chapter 2 – Air Quality

- *Is the discussion on O_3 and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate and complete? If not, what additional information needs to be included?*

The last sentence of the first paragraph of Chapter 2 lists 4 important factors that affect concentration of ozone and other photochemical products. Deposition to surfaces should be added as a 5th factor, as it has a strong effect on ambient ozone concentrations.

The sentence on lines 31-33 of page 2-2 is not correct. It would be accurate if revised to read: "This mechanism is similar to the chemistry driving summertime O_3 formation, although the photolysis of VOCs is a more important primary radical source in winter. In summer, the major primary radical source is the photolysis of O_3 to form an excited state O atom, which then can react with water to form OH radicals."

- *Is the discussion on Sources and Emissions of O_3 Precursors (Section 2.2) accurate and complete? If not, what additional information needs to be included?*

As I have stated in previous responses, the uncertainty of the ozone precursor emissions estimates should be clearly discussed and defined to the extent possible. This section gives no indication of the precision and accuracy of the estimates, except the total emissions of the precursor classes are given to 5 significant figures, which is misleading. I think that a paragraph should be included that discusses emission inventory uncertainty. One example of inventory uncertainty is the differences in emissions between those discussed in Section 2.2 and those actually used in the photochemical modeling discussed in Appendix 3C. (This comment largely repeats a comment that I made in my response to a similar question regarding the PM PA; more details are given there.)

- *Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3) accurate and complete? If not, what additional information needs to be included?*

I find the discussion in this section to be accurate and complete.

- *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what additional information needs to be included?*

The discussion in this section is reasonably accurate and complete, but there are some subtleties that should be discussed to more clearly inform the reader. In Figure 2-5 relatively large symbols are used for each monitor color coded to indicate the 2015-2017 design values. The points with the largest design values are plotted last, so in urban areas with many monitors, one can only see the monitors with the largest design values. As a consequence, the plot gives a somewhat biased picture. If this figure used smaller symbols, the bias would at least be partially corrected. Figure 2.6 has a similar bias with larger

symbols plotted last indicating the largest decreases, and smaller decreases and increases plotted first and with smaller symbols.

The conclusions drawn from Figures 2-7 and 2-8 do not adequately reflect the tremendous success of the U.S. effort to reduce ambient ozone concentrations. Figure 2-7 does accurately show that there has been a 32% decrease in U.S. annual 4th highest MDA8 levels since 1980, but that 32% does not consider the U.S. background ozone concentration that emission controls cannot directly affect. Parrish et al. (2017) and Parrish and Ennis (2019) show that when the percent decrease is based on the enhancement of those levels above what would be present from U.S. background ozone alone, then the percent decrease since 1980 is >80% (i.e., a decrease of more than a factor of 5). As the discussion notes, "the trend in the annual 4th highest MDA8 concentrations has been relatively flat since 2013, and the design values have been relatively constant since 2015." The primary reason for this behavior is that there is not much room left for improvement: < 20% of the 1980 enhancement above background. In my view this issue should be emphasized in the discussion of Figures 2.7 and 2.8 as well as in a similar plot in Figure 2-14.

The discussion of Figure 2-9 emphasizes that the five eastern U.S. regions have all shown decreases of at least 10 ppb in median annual 4th highest MDA8 values since the early 2000's, while the four western U.S. regions have all shown decreases of less than 10 ppb. It should be emphasized that this is primarily due to the eastern regions having, on average, more anthropogenic ozone in the early 2000s, which could be reduced., than in the western U.S. The reason this is not so obvious from figure 2-9 is that the U.S. background ozone is higher in the west. If that figure showed the enhancement of the 4th highest MDA8 values above the 4th highest MDA8 values that would be present from U.S. background ozone alone, then this point would be more obvious.

In Figures 2-10 and 2-11, the meaning of the boxes, lines and points should be explicitly stated as done in Figure 2-12.

The paragraph on lines 11-17 of page 2-19 reads: "Panel B shows the seasonal pattern for an urban site in Baton Rouge, LA. Throughout the southeastern U.S., the highest O_3 concentrations are often observed in April and May due to the onset of warm temperatures combined with abundant emissions of biogenic VOCs at the start of the growing season. This is often followed by lower concentrations during the summer months, which is associated with high humidity levels that tend to suppress O_3 formation. Some areas, particularly in the states bordering the Gulf of Mexico, may experience a second peak in O_3 concentrations in September and October." My understanding of the double peak behavior of ozone along the Gulf coast is that a particular meteorological pattern (i.e., the development of the Bermuda High) brings cleaner Gulf of Mexico air into the region during the mid-summer months, and more polluted continental air into the region before and after those months. I am not aware of any mechanism by which high humidity levels tends to suppress O_3 formation.

- *Is the discussion on Background O_3 (Section 2.5) accurate and complete? If not, what additional information needs to be included?*

(Note: some of the material here is similar to my responses to questions regarding background ozone in the O_3 ISA.)

In my view the perspective of this entire discussion should be changed. Over the U.S., the large majority of ambient ozone concentrations comes from background sources. Ozone produced from U.S. anthropogenic precursor emissions account for relatively minor, but important, enhancements of ozone concentrations above the concentrations that would be present from USB ozone alone. These enhancements are relatively large in urban areas, which account for ozone exceedances occurring primarily in urban areas. Understanding U.S. ambient ozone concentrations from this perspective would provide a useful basis for air quality policy development.

Footnote 17 is incorrect. Ozone concentrations that do not include contributions from U.S. anthropogenic emissions can indeed be determined exclusively from O_3 measurements (see Parrish et al., 2017; Parrish and Ennis, 2019), although it is true that they cannot be directly measured.

Figure 2-15b is misleading. The second example (Ex 2) is meant to acknowledge that background ozone can be a large contributor to ozone concentrations at some sites, even when the MDA8 ozone concentration exceeds the NAAQS. However, the figure understates the possible contribution of U.S. background ozone. For example, Figure 3 of Jaffe et al. (2018), which is reproduced as Figure 2 below, suggests that U.S. background ozone alone can give ozone design values that exceed 60 ppb over most of the southwestern U.S. An observationally based approach for estimating ozone design values from USB ozone alone (Figure 3 below) gives a similar indication. This is a critical issue that must be faced when attempting to reduce design values to a NAAQS of 70 ppb or lower. Example 2 of Figure 2-15b should be revised to more clearly show the difficulty of this situation.

Section 2.5.1.6 on Post-Industrial Methane has some shortcomings. It is true that in "The U.S. and the rest of the world anthropogenic methane emissions have not been tracked quantitatively in detail until relatively recently." However, it does not follow that "As a result, the pre-industrial methane concentration is relatively unconstrained." Pre-industrial methane concentrations are firmly established from measurements of methane trapped in air bubbles in ice cores.

Section 2.5.1.6 on Post-Industrial Methane should also emphasize that the role methane plays in the determining global tropospheric ozone concentrations has been quantified only by chemistry-climate model simulations. That dependence is expected to be critically dependent upon the model-derived global NOx concentration distribution, and the model simulations of that NOx distribution are quite sensitive to parameterizations of many physical processes within the models. The parameterizations have been tested by observation-model comparisons only to a limited extent, so their success in realistically simulating the physical processes remains uncertain. Finally, the NOx concentration distribution is poorly characterized from the limited measurements available, and the measured concentrations are often at or below the detection limit of the instruments making the measurements. Thus, in my opinion, increasing methane may indeed increase global ozone concentrations, but due to model uncertainties that relationship is uncertain. Conceivably increasing methane may decrease, rather than increase, global ozone concentrations. The uncertainty regarding methane's role should be made clear.

Section 2.5.2.2 – Methodology: Strengths, Limitations and Uncertainties - discusses uncertainties in model estimates of USB. The final concluding sentence is "As a single estimate, this study relies upon the literature based (estimate of USB uncertainty of) ±10 ppb for seasonal means (Jaffe et al., 2018)." However, Jaffe et al. (2018) go on to add the phrase "…and higher for individual days." Since the design value is based on 4 individual days, the USB contribution to the design value fall in the "higher than ±10 ppb category. It would be informative to present model-measurement comparisons for the ODVs recorded at relatively isolated rural CASTNET sites in the southwestern U.S. The influence of U.S. anthropogenic ozone contributions at the sites shown in Figure 1 are minimal, so a comparison of the ODVs calculated in the ZUSA simulation with those observed may be straight forward.

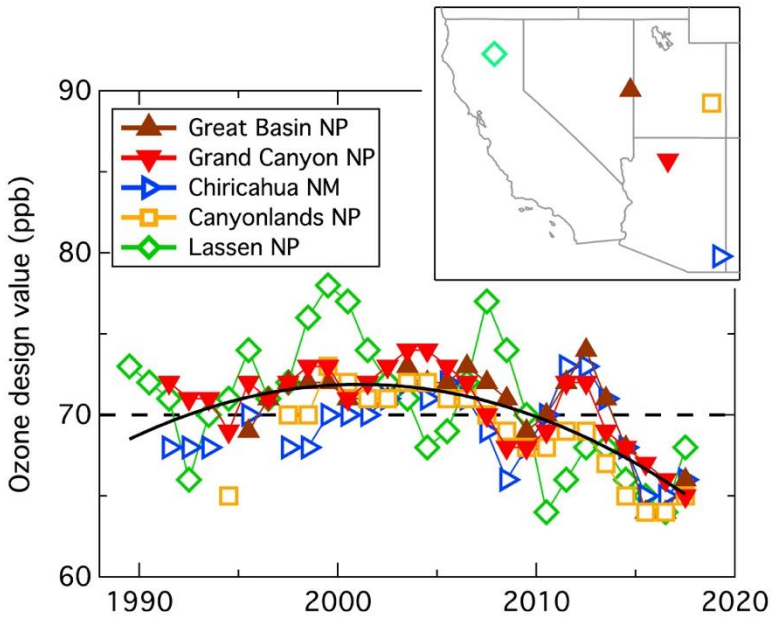


Figure 1. Ozone design values recorded at five relatively isolated CASTNET sites in the southwestern U.S. (Data from EPA's AQS data archive (https://www.epa.gov/aqs).

Figures 2.16 and 2.17 are informative plots. Evidently the minimum and maximum that are given are not minimum or maximum simulated on any day in each season, but are instead the minimum and maximum mean MDA8 O_3 concentration simulated for any grid cell in the domain. This should be clarified.

Figure 2-22 seems to indicate that MDA8 ozone from natural sources can exceed 70 ppb on many days in the western U.S. and even on some days in the eastern U.S. Does this not imply that natural sources alone can give an ozone design value larger than the current NAAQS of 70 ppb, at least in the western U.S.? The right center panel of Figure 2-27 shows that this is indeed the case, with the maximum 4th highest US background O_3 simulated day of 80 ppb. Does this not imply that it is impossible to reach the current NAAQS of 70 ppb through domestic precursor emission controls only? Further, that figure shows that ozone design values can be above ~60 ppb from US background ozone alone over much of the western U.S. This map is roughly similar to the maps that I included in my response to questions regarding the O_3 ISA, and are reproduced here as Figures 2 and 3. These three figures from two model calculations and one observational based analysis show how difficult it is to reach even a 70 ppb NAAQS in large regions of the country. This issue deserves full discussion in this chapter. The final conclusion of this section is a good start for this recommended full discussion: "…a combination of Natural and Canada/Mexico contributions can lead to total USB between 60-80 ppb on specific days, ….".

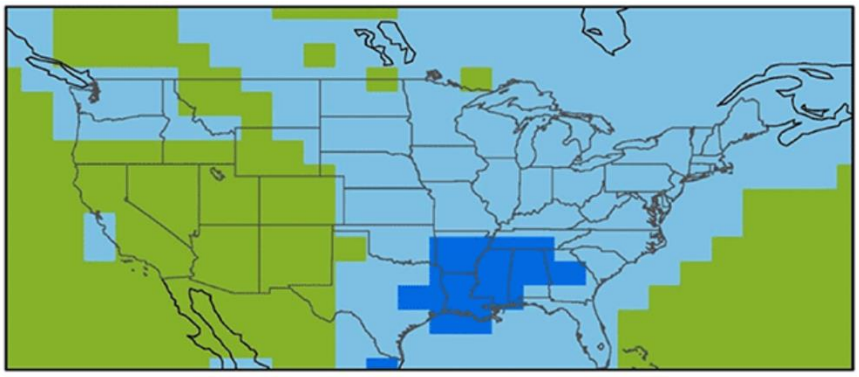


Figure 2. Annual 4th highest MDA8 O_3 in ppb from North American background (i.e., with North American anthropogenic precursor emissions set to zero) averaged over 2010–2014 from a GFDL-AM3 model simulation (Jaffe et al., 2018).

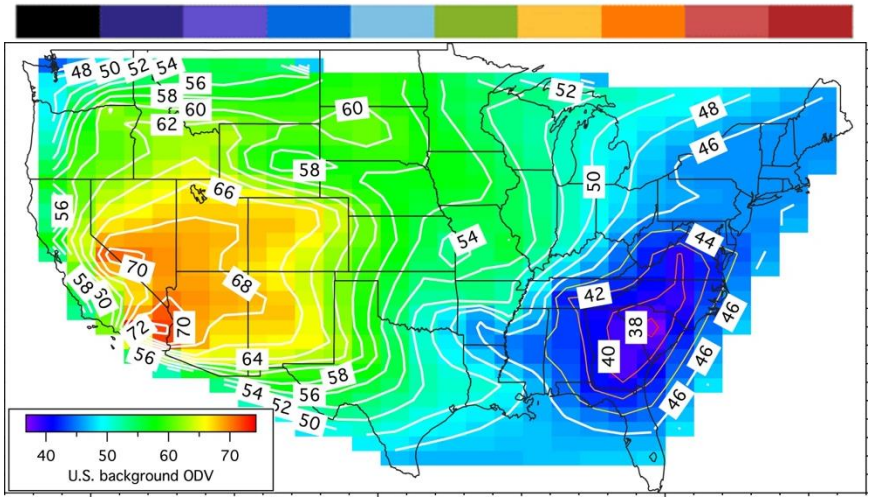


Figure 3. Ozone design values expected from U.S. background (i.e., with U.S. anthropogenic precursor emissions set to zero) in ~ 2015 derived from observations (D.D. Parrish, unpublished figure).

Chapter 3 – Review of the Primary Standard

- *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section 3.4.1) accurate and complete? If not, what additional information needs to be included?*

I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.

- *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard (Section 3.4.2) accurate and complete? If not, what additional information needs to be included?*

I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.

- *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be included?*

I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.

- *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what additional information needs to be included?*

I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.

- *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not, what additional information needs to be included?*

I have no relevant expertise in evaluating public health implications, so I cannot respond to this question.

Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses

- *Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what additional information needs to be included?*

Very limited summary data for each urban area are given in Table 3C-1. I have not independently checked those data, but they appear to be accurate and complete.

- *Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete? If not, what additional information needs to be included?*

This section simply describes the data which were downloaded from the EPA's Air Quality System (AQS) database; the discussion appears to be accurate and complete.

- *Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1) accurate and complete? If not, what additional information needs to be included?*

I do not have experience with performing photochemical model simulations. To me the discussion of CAMx appears accurate, as expected, since this section is simply a discussion of how a widely-used photochemical model was setup for the application described in this Appendix.

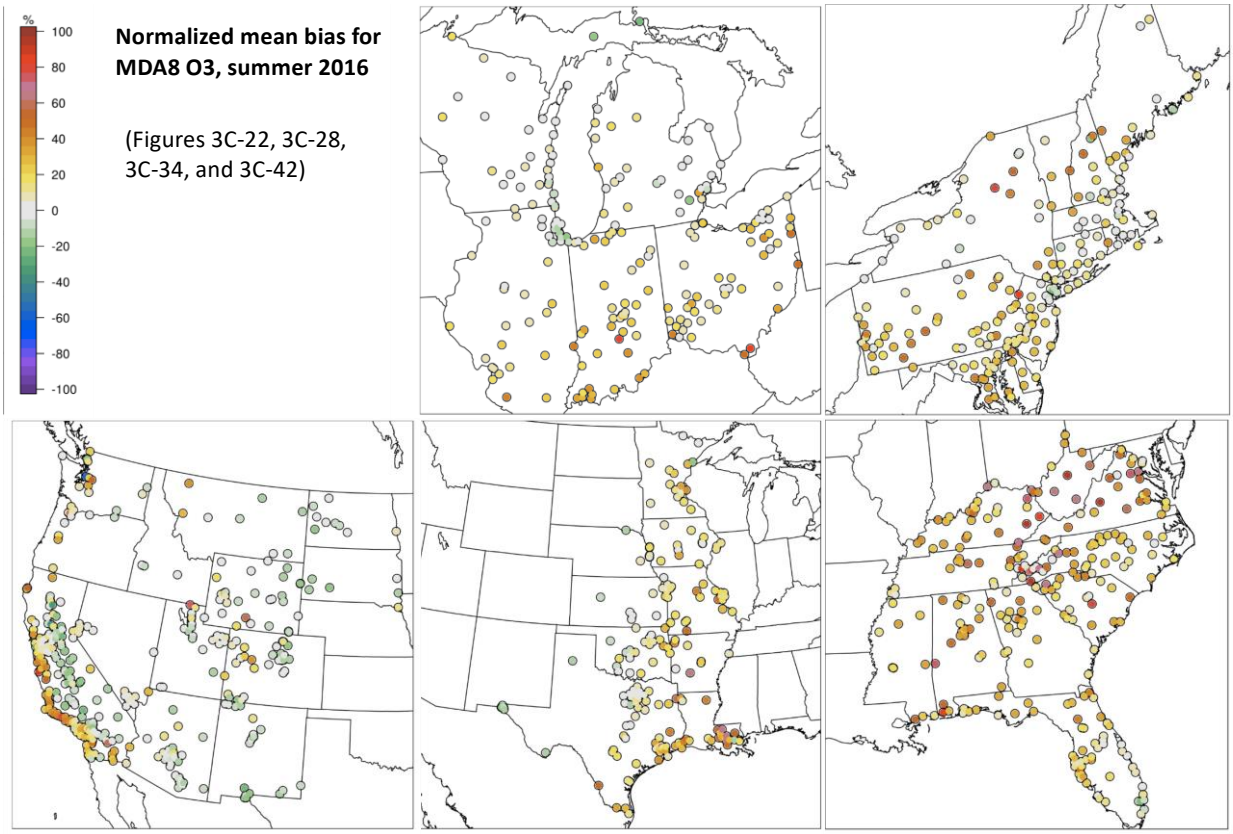
One issue that is always relevant for model calculations is the accuracy of the emission inventory. A paragraph discussing how the emissions assumed for this model compare with other measures of U.S. emissions would provide useful information. For example, a quick comparison between the total emissions in Table 3C-4 with the total emissions given in the pie charts in Figure 2-1 shows some similarities and some surprising differences. For CO, both the anthropogenic and natural components are in close agreement. For VOCs, the anthropogenic components agree well, but in the CAMx inventory the biogenic VOCs are larger by about 11%. Surprisingly, the anthropogenic NOx emissions are about 20% smaller in the CAMx inventory. These differences are certainly within the uncertainty of the inventories, but even these small differences may have an effect on the modeling results. The difference in anthropogenic NOx emissions may be particularly important in this particular modeling study, because NOx emissions are the parameter adjusted in the Air Quality Adjustments in Section 3C.5. A parameter that modelers often use to explain features of atmospheric photochemistry is the VOC to NOx ratio. In the CAMx inventory (Table 3C-4) this ratio (on a wt:wt basis) is about 5.1 compared to 3.9 in

the NEI Inventory (Figure 2-1), based on the total emissions. It would be useful to discuss the impact of this difference in VOC to NOx ratio, along with any other significant uncertainties in the emissions that might impact the results.

As second issue that affects the results of the modeling is the accuracy of the boundary conditions calculated by the hemispheric version of the Community Multi-scale Air Quality model (H-CMAQ) v5.2.1. These boundary conditions account for the majority of the ozone throughout the modeling domain; thus, the accuracy of all of the results of this modeling exercise depends on the accuracy of the boundary conditions. A comparison of the modeled ozone concentrations at CASTNET sites, particularly in the western U.S. (as shown in Figure 1 above), would give an insightful indication of their accuracy. A zero-out model run with all U.S. anthropogenic emissions set to zero should be conducted to calculate U.S. background ozone, and the results compared with other determinations of U.S. background ozone (also see maps in Figures 2 and 3 above).

- *Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and complete? If not, what additional information needs to be included?*

This section contains 33 pages with 13 Tables and 36 Figures, many with multiple panels. More numbers and graphs are not needed for completeness, but a better synthesis of the results would be useful. Figures could be combined to allow an easier approach to that synthesis. For example, the following figure combines 5 figures from the report so that a reader can easily compare and contrast results across the country. The discussion of these results could then be more concise and insightful.



Much more of this nature could be done to increase the value of this section. Another example is figures of the style 3C-17; instead of time series of hourly data, it would be useful to plot all observed and modeled hourly data in one 24-hour span, with means and standard deviations of each indicated, much as in Figure 3C-67 and following figures. Such plots would much better inform the reader regarding possible causes of model-observation differences.

I am not an expert in modeling, so I cannot critique the modeling procedures described in this section. I have not identified any inaccuracies or incompleteness in the description of the modeling. However, to my mind this section is incomplete in two regards. First, an overview of the reasons for choosing the emissions adjustments (NOx emission reductions alone) used in this section should be given. Figure 3C-48 is a flow diagram demonstrating the HDDM model-based O_3 adjustment approach. One part of Step 3 is to select emissions reductions to which sensitivities will be applied. How are these reductions selected? Throughout this section, only NOx emissions are reduced, but in the real world, anthropogenic VOC emissions are reduced simultaneously with NOx reductions. The introduction to this section should give the reader some idea of what guided the choices made during this modeling exercise. Second, a discussion of the likely uncertainties of the final results should be given.

- *Is the discussion on Air Quality Adjustment to Meet Current and Alternative Air Quality Scenarios (Section 3C.5) accurate and complete? If not, what additional information needs to be included?*

I can identify one zero-order test of the accuracy of the final outcome summarized in Table 3C-19; if I understand correctly, this table gives the percent reductions of anthropogenic NOx emissions required to lower the 2017 ozone design values to just meet three air quality scenarios. For Phoenix to reach a design value of 65 ppb, NOx emissions would have to be reduced by 68% (all other emissions remaining constant). However, the ODV that would be recorded in the absence of all U.S. anthropogenic precursor emissions would likely be above 65 ppb in 2017 (see maps in Figures 2 and 3 above). In that case it would not be possible to lower the ODV to 65 ppb in Phoenix. In my opinion the modeling approach described in this section is probably state-of-the-art work, but the uncertainty of the results is large. This modeling uncertainty should be thoroughly discussed in this Section.

Apparently, there are some unrealistic results included in the summary plots and tables; I suggest that they be removed. For urban areas that already had design values below 75 ppb in 2017, modeling was done for NOx emission **increases** necessary to **raise** the design values up to 75 ppb (Table 3C-19). This may be a modeling exercise that is useful for completeness, but is simply confusing to at least this reader. Figures like the left panel of Figure 3C-84 should not be included. Similarly, for the respective panes in Figures 3C-91 through 3-114.

- *Is the discussion on Interpolation of Adjusted Air Quality using Voronoi Neighbor Averaging (Section 3C.6) accurate and complete? If not, what additional information needs to be included?*

The discussion in Section 3C.6 appears accurate to me. What is missing is a discussion of the uncertainty of this approach. I suggest that several trials be run for some of the 8 urban areas to approximately quantify the uncertainty. Each trial would select a census tract that actually has a monitor to provide a time-series of "known" concentrations. Then the interpolation of that census track concentration using Voronoi neighbor averaging would be calculated, but without including data from the census track monitor; this would provide "interpolated" concentrations. A comparison of the "known" versus "interpolated" concentrations for the subject census tract would be illuminating regarding the accuracy of this procedure.

- *Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not, what additional information needs to be included?*

This section has an effective and complete presentation of the results. In each of the eight panels in Figures 3C-107 through 3C-114, I suggest that the average, population-weighted annual 4th highest MDA8 O_3 or May-September mean MDA8 O_3 be indicated in annotations.

In my opinion, the summary sentence for this section is inadequate. It currently reads "In summary, these figures show that using the CAMx/HDDM adjustment methodology, peak O_3 concentrations are reduced in urban areas with large domain wide reductions in U.S. anthropogenic NOx emissions." I think that a statement should be added to the effect that the total population weighted average ambient MDA8 ozone concentrations decrease with emission reductions designed to reduce the annual 4th highest MDA8 O3 concentration. The success of the U.S. program in reducing ambient ozone concentrations requires emphasis, regardless of whether the NAAQS has been, or even can be, reached in some urban areas.

Questions from Dr. Sabine Lange

Air Quality

1) *Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time, over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are your thoughts about the change of annual average ozone concentrations (which tend to be the focus of epidemiology studies) with decreases in annual peak ozone concentrations?*

The general situation exemplified in Figure 1 is more or less typical of the temporal evolution of urban ozone concentration distributions, where maximum daily 8-hour average (MDA8) ozone concentrations have decreased, but the minimum MDA8 values have increased. This causes the distribution of MDA8 ozone concentrations to narrow, as shown in the figure. The cause of the increase in the minimum MDA8 ozone concentrations is a reduction in fresh NO emissions in the urban area. The effect of these emissions on days of low photochemical activity is for NO to react with ozone, forming NO_2. Thus, between the early 2001-2003 period and the later 2013-2015 period, on days of low photochemical activity the MDA8 ozone concentrations have increased but the NO_2 concentrations have decreased. Since the mean and median MDA8 have not changed significantly over this time interval, it may well be that the annual average ozone concentrations have not changed much. The possibility that annual average ozone concentrations have not changed, but that NO_2 concentrations have decreased, would be important to consider in the interpretation of epidemiology studies that focus on annual average ozone concentrations.

Epidemiology

2) *Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?*

I have no relevant epidemiological expertise, so I cannot respond to this question.

3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg. 3-40 and pg. 3-43). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?*

I have no relevant epidemiological expertise, so I cannot respond to this question.

Exposure-Response Modeling

4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?*

I have no relevant health effects expertise, so I cannot respond to this question.

5) *The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?*

I have no relevant health effects expertise, so I cannot respond to this question.

Questions from Dr. Corey Masuca

1) 2.1. Ozone and Photochemical Oxidants in the Atmosphere

How sound science is this mechanism of ozone transfer between the stratosphere and the troposphere?

The scientific evidence that ozone transfer from the stratosphere to the troposphere occurs in stratospheric intrusions associated with tropopause folds is very strong. The science that underlies our understanding of the injection of stratospheric intrusions into the troposphere, their transport within the troposphere, and their dispersion into the background troposphere is also strong, because it is based on our understanding of meteorology, which has a long history of extensive research. The work by Langford et al. (2018) is a good example of the state-of-the-art of our ability to use observations and transport modeling to characterize the impact of a specific stratospheric intrusion event.

A second mechanism for stratosphere to the troposphere exchange occurs over northern mid-latitude continents, where strong convection associated with thunderstorms penetrates to the stratosphere, and brings stratospheric air into the troposphere. I believe that less research has been devoted to this mechanism, but on a global scale it is thought to have a smaller impact than tropopause folding events. Ultimately, it would be valuable to be able to accurately quantify the contribution that ozone from the stratosphere makes to observed surface ozone at any particular time and place; the science is not yet advanced enough for this to be possible. Models can provide partial answers (e.g., Langford et al., 2017) but the accuracy of those answers is not well quantified.

2) 2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks

While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET, National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road Monitoring Sites, especially for NOy?

As of September, 2019, there were apparently 82 Near Road Monitoring Sites in many states throughout the U.S. (https://www3.epa.gov/ttnamti1/nearroad.html) that operated for at least some period of time. The goal of this network is to quantify NO_2 concentrations in the near field of vehicle emissions. As far as I know, there is no emphasis on measurement of NOy at these sites. Adding a brief discussion of this network to Section 2.3.1 would be useful.

3) 2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards Are Met

There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is this short-term 8-hour rolling average consistent with short-term actual and scientific studies?

The maximum of the 8-hour rolling averages (MDA8) recorded on a given day is useful for scientific studies. On sunny days that usually experience the largest ozone concentrations, this average generally characterizes the ozone concentration during the period of the day when 1) the largest ozone concentrations have accumulated, and 2) when the convective boundary layer is well developed.

4) 2.4.3 Diurnal Patterns

While this section refers diurnal patterns of relative ozone concentrations between day and night, are these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant weather conditions? What about the effects on topography/geography in determining diurnal patterns?

The diurnal pattern of ozone at surface sites is driven by several processes. The influence of each factor at a particular site varies depending upon the characteristics of each site, so each site has its own characteristic diurnal pattern.

At most sites in relatively flat terrain, the most important factor is usually the evolution of the convective boundary layer. At night during relatively calm wind periods, the boundary layer is shallow (nominally 10s of meters to ~100m). Ozone is lost to surfaces, and this surface deposition can reduce surface ozone to low concentrations within this shallow layer, which includes the ozone monitor. In areas with significant surface NOx emissions, reaction of ozone with freshly emitted NO also contributes to the depletion of near-surface ozone. After sunrise, solar radiation heats the surface, initiating convection that in the morning hours increases the depth of the boundary layer by entraining air from aloft. This air was above the nocturnal boundary layer, so its ozone concentration has not changed appreciably overnight; surface ozone concentrations increase due to this entrainment.

A second important factor is photochemical production of ozone from precursors contained in the boundary layer. The contributions to the ozone increase from entrainment of air aloft and photochemical production within the boundary layer are not easily distinguished from measurements, since both processes are occurring simultaneously.

A third factor is advection (horizontal transport) of air to the site. If there is an urban area upwind, then rural ozone may increase later in the afternoon, when urban pollution ozone is finally advected to the site.

These three factors are each affected by temperature during the day (with higher temperature generally favoring both faster boundary layer growth and faster photochemical ozone production) and meteorology including the degree of stagnation (which affects boundary layer growth and advection).

Finally, topography/geography does play a major role. For example, on a mountaintop the nocturnal boundary layer generally does not form and there is usually only small precursor concentrations, so the diurnal pattern is much flatter than at a site in flatter terrain.

Thus, it is difficult to give a simple explanation of diurnal ozone patterns. The discussion of Figure 2-10 in this section gives a reasonably accurate overview.

5) Background Ozone

There, in general appears to be a lot of discussion about background ozone concentrations from transport and natural sources. However, are most salient ozone concentrations more localized and from anthropogenic sources?

The short answer is no. As I noted in my comments on Section 1.8 of the ISA on U.S. background ozone concentrations, at present U.S. background ozone contributes the majority of urban ozone concentrations, even on most days when ozone exceeds the NAAQS. The figures in Section 2.5 of the PA agree with this statement. In my response to a question on background ozone that was posed during the review of the ISA, I included two contour maps showing estimates of USB across the country, one from a model calculation and one from an observational based analysis. They are reproduced above as Figures 2 and 3. Broadly speaking the two maps agree that the ozone design value that would be measured in the absence of U.S. anthropogenic emissions of ozone precursors would vary from ~40 ppb to ~70 ppb, with the larger values in the southwest and the lower values in the southeast. During exceedance episodes, the more localized ozone concentrations from anthropogenic sources can usually be conceptually viewed as a relatively smaller contribution that raises the U.S. background ozone concentration above the NAAQS.

This section references the utilization of photochemical grid models due to the lack of ability to characterize the origins of ozone and the ability to estimate the magnitude of background ozone. However, how predictable are these photochemical models, especially given the highly photolytic and relative instability of ozone in the atmosphere?

The results from photochemical grid model simulations have poorly quantified uncertainties. However, these uncertainties are relatively large compared to the margin between the NAAQS and the observed ozone design values in most nonattainment areas of the country. For example, Jaffe et al. (2018) estimates that the uncertainty in U.S. background ozone concentrations calculated by models is around ±10 ppb for seasonal mean values and higher for individual days. Attainment vs. nonattainment decisions are often based on ozone concentration differences that are smaller that this uncertainty. The U.S. EPA recognizes that the absolute ozone concentrations simulated by models have significant

uncertainties, so the use of Relative Response Factors (RRF) are recommended during the development of state implementation plans (for example, see https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&dirEntryId=306790). The RRF approach assumes that models can accurately calculate the response of ambient ozone concentrations to precursor emission changes, even while the model cannot accurately calculate the absolute ozone concentrations. In looking through the ozone ISA and PA, I find no discussion of the RRF approach, which I believe is a major shortcoming of these documents.

This section mentions that international emissions sources via transport mostly originate from anthropogenic sources. However, is there a possibility that there can be international transports from non-anthropogenic/biogenic sources?

Also, this section noticeably leaves out non-international, interstate transport of ozone.

International transport from non-anthropogenic/biogenic sources is extremely important. Ozone from stratospheric intrusions and ozone precursors from wild fires are two very important examples. I think that the discussion of the U.S. background correctly focuses on the international transport because non-international, interstate transport of ozone is adequately treated in the regional photochemical modeling.

6) 2.5.1.6 Pre-Industrial Methane

There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance of methane with respect to the formation of and consideration of ozone? Is a discussion on methane warranted?

Methane as a participant in atmospheric photochemistry and may well make a significant contribution to U.S. background ozone concentrations. Section 2.5.1.6, which constitutes about 1 page of the 64-page chapter, is I think warranted.

References

Jaffe D. A., et al. (2018) Scientific assessment of background ozone over the U.S.: Implications for air quality management. *Elem. Sci. Anth.,* 6 56 doi.org/10.1525/elementa.309.

Langford, A. O., et al. (2017), Entrainment of stratospheric air and Asian pollution by the convective boundary layer in the southwestern U.S., *J. Geophys. Res. Atmos., 122*, 1312–1337, doi:10.1002/2016JD025987.

Langford, A. O., et al. (2018). Coordinated profiling of stratospheric intrusions and transported pollution by the Tropospheric Ozone Lidar Network (TOLNet) and NASA Alpha Jet experiment (AJAX): Observations and comparison to HYSPLIT, RAQMS, and FLEXPART, *Atmos. Environ.*, 174, 1-14, https://doi.org/10.1016/j.atmosenv.2017.11.031.

Parrish, D. D., Young, L. M., Newman, M. H., Aikin, K. C., and Ryerson, T. B. (2017) Ozone Design Values in Southern California's Air Basins: Temporal Evolution and U.S. Background

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Parrish, D. D. and C. A. Ennis (2019). Estimating background contributions and US anthropogenic enhancements to maximum ozone concentrations in the northern US, *Atmos. Chem. Phys., 19*, 12587–12605, https://doi.org/10.5194/acp-19-12587-2019.

Dr. Sonja Sax, Ramboll

Questions from Dr. Corey Masuca

1) 2.1. Ozone and Photochemical Oxidants in the Atmosphere

How sound science is this mechanism of ozone transfer between the stratosphere and the troposphere?

> I am not sufficiently familiar with these transport mechanisms to adequately answer this question.

2) 2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks

While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET, National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road Monitoring Sites, especially for NOy?

> I agree that any data or information from the Near Road monitors should be included and discussed.

3) 2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards Are Met

There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is this short-term 8-hour rolling average consistent with short-term actual and scientific studies?

> This is an important question that has been raised by others (e.g., Dr. Lange). In general, I don't think there is clear agreement between how the NAAQS design values are calculated (for determining whether an area is in compliance with the NAAQS) and how exposures are evaluated in the epidemiological literature. In addition, there is also some discordance between how exposures are evaluated in controlled human exposure studies and animal studies, and how the NAAQS is determined from monitoring stations. My colleagues and I discuss this and related issues in the following publication:
>
> Goodman, JE; Sax, SN; Lange, SS; Rhomberg, LR. 2015. "Are the Elements of the Proposed Ozone National Ambient Air Quality Standards Informed by the Best Available Science?" *Reg. Tox. Pharmacol.* 72(1):134-140.

4) 2.4.3 Diurnal Patterns

While this section refers diurnal patterns of relative ozone concentrations between day and night, are these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant weather conditions? What about the effects on topography/geography in determining diurnal patterns?

EPA does a good job in summarizing information related to not only diurnal patterns, but also regional patterns where specific weather conditions (such as stagnant weather patterns) and/or topography could impact ozone concentrations (i.e., based on the selection of examples provided as in Figures 2-10 and 2-11). While additional discussion could be included to specifically address these points, the examples provided show a good range of different conditions that could impact ozone concentrations spatially and regionally.

5) Background Ozone

There, in general appears to be a lot of discussion about background ozone concentrations from transport and natural sources. However, are most salient ozone concentrations more localized and from anthropogenic sources?

I appreciate that EPA includes a thorough discussion of background sources of ozone because in some regions of the country, background ozone levels can be a significant contributor to overall ozone levels, and this makes it challenging to meet increasingly more stringent NAAQS. Understanding when and how much background ozone contributes to overall ozone levels will help in attainment of the NAAQS.

This section references the utilization of photochemical grid models due to the lack of ability to characterize the origins of ozone and the ability to estimate the magnitude of background ozone. However, how predictable are these photochemical models, especially given the highly photolytic and relative instability of ozone in the atmosphere?

I am not sufficiently familiar with the photochemical models to comment on this question.
This section mentions that international emissions sources via transport mostly originate from anthropogenic sources. However, is there a possibility that there can be international transports from non-anthropogenic/biogenic sources?

I agree that it is possible for international transport of biogenic precursors to also contribute, but it may be more difficult to evaluate the contributions from these sources.

Also, this section noticeably leaves out non-international, interstate transport of ozone.

I agree that this is an important issue that should be addressed.

6) 2.5.1.6 Pre-Industrial Methane

There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance of methane with respect to the formation of and consideration of ozone? Is a discussion on methane warranted?

I am not sufficiently familiar with all the details regarding ozone chemistry, if it does play a significant role in ozone formation, then I think it is appropriate for methane to be discussed.

Questions from Dr. Sabine Lange

Air Quality

1) *Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have demonstrated that in an area where peak daily ozone concentrations have decreased over time, over the same period of time the lowest daily ozone concentrations have also decreased (due to the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are your thoughts about the change of annual average ozone concentrations (which tend to be the focus of epidemiology studies) with decreases in annual peak ozone concentrations?*

   EPA does acknowledge that "Reductions of NOX emissions are expected to result in a compressed O3 distribution, relative to current conditions" (Draft Ozone PA, pg. 2-4), and it looks like that is what is shown in Dr. Lang's Figure 1. As Figure 1 shows, however, this also means that there will be more days that experience somewhat higher ozone concentrations, although potentially no days with levels that exceed very high concentrations. With regards to how these changes should be interpreted for epidemiology studies, I think the larger issue of how ambient levels relate to actual personal exposures of ozone and how this impacts exposure measurement error in the epidemiology studies is a more critical issue. In the PA, EPA acknowledge this important source of uncertainty, and is one reason provided for not conducting the "epidemiology-based" risk assessment.

Epidemiology

2) *Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?*

   The issue of statistical power is separate from issues related to confounding, errors and bias. You can have a very large study that has serious confounding issues if these are not controlled for (or are unmeasured). Similarly, large studies can be prone to selection bias, exposure measurement errors, etc. Sample size (or statistical power) will affect whether you are able to "detect" an effect, and is only one aspect of study quality (larger sample sizes are preferred), but is separate from other issues of study quality, which are associated with the study design, execution, and analyses methodology. That is, poor study design, execution or poor methodology can lead to errors and biases.

3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40 and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?*

I agree with this statement – the ambient data, whether from fixed-site monitors or from modeling data are only surrogates of the actual personal exposures and any differences contribute to exposure measurement errors. This statement is true for all air pollution studies, not only ozone, and this caveat should be included for other air pollution epidemiology studies.

Exposure-Response Modeling

4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?*

   This approach does not make sense to me. If asthmatics are truly more susceptible to the effects of ozone, then it might be that the threshold for effects might be lower, but not zero. Although data are limited, the data that are available do not indicate that asthmatics are more susceptible than non-asthmatics to the effects of ozone. In fact, data are inconsistent, with some studies indicating effects in asthmatics at elevated ozone exposures, but others showing no effects. For example, no effects on lung function were observed in asthmatics compared to non-asthmatics at exposures to 400 ppb for 2 hours (Alexis *et al*., 2000) and 200 ppb for 2 hours (Mudway *et al*., 2001).

   Alexis, N; Urch, B; Tarlo, S; Corey, P; Pengelly, D; O'Byrne, P; Silverman, F. 2000. "Cyclooxygenase metabolites play a different role in ozone-induced pulmonary function decline in asthmatics compared to normals." *Inhal. Toxicol.* 12(12):1205-1224.

   Mudway, IS; Stenfors, N; Blomberg, A; Helleday, R; Dunster, C; Marklund, SL; Frew, AJ; Sandstrom, T; Kelly, FJ. 2001. "Differences in basal airway antioxidant concentrations are not predictive of individual responsiveness to ozone: A comparison of healthy and mild asthmatic subjects." *Free Radic. Biol. Med.* 31(8):962-974.

5) *The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?*

   The controlled human exposure studies that form the basis of the exposure-response model are based on exposure circumstances that are highly unlikely to occur in the general population, and in particular in susceptible population groups (i.e., heavily

exercising individuals exposed to elevated concentrations of ozone over extended periods of time). Only outdoor workers are likely to experience the exposure conditions in these studies. In addition, the results clearly indicate that only a small percentage of the study volunteers (although generally healthy adults) had a statistically significant response to ozone, and as noted by Dr. Lange, these responders likely represent people that are more susceptible to ozone (particularly at lower ozone concentrations). Therefore, I agree that the model already represents a very conservative estimation of ozone effects that are likely to be protective of sensitive population groups.

Questions from Dr. James Boylan

Chapter 2 – Air Quality

- *Is the discussion on O_3 and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Sources and Emissions of O_3 Precursors (Section 2.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Background O_3 (Section 2.5) accurate and complete? If not, what additional information needs to be included?*

Overall, for the PA, the discussion of Air Quality seemed accurate and complete. As noted by other CASAC members, inclusion of state-to-state transport of ozone and ozone precursors could be included, in addition to a discussion of potential international transport of non-anthropogenic precursors of ozone.

Chapter 3 – Review of the Primary Standard

- *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section 3.4.1) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard (Section 3.4.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not, what additional information needs to be included?*

In general, the overall summary of the Review of the Primary Standard was adequate for the PA. The modeling of the Population and Exposure Risk Assessment (which I only briefly reviewed) appeared to be very extensive and thorough, although I did not see any of the actual estimates of the individual exposures, which would have been interesting to see. Also, it would be interesting to compare the modeled estimates to actual personal exposure studies to provide some validation for the model (I did not see any discussion of model validation).

Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses

- *Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Air Quality Adjustment to Meet Current and Alternative Air Quality Scenarios (Section 3C.5) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Interpolation of Adjusted Air Quality using Voronoi Neighbor Averaging (Section 3C.6) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not, what additional information needs to be included?*

In general, these sections of the PA appeared to be adequate and complete. I did not review in detail to assess whether the information is accurate, as that would be beyond my available time and expertise. The results and discussion seemed appropriate.

Dr. Duncan Thomas, University of Southern California

Questions from Dr. Sabine Lange:

Air Quality

Not my area of expertise.

Epidemiology

1) *Is an epidemiology study with higher statistical power (sample size) innately more protected against problems of confounding, error, and bias, than an epidemiology study with lower statistical power (sample size)?*

> **Response**: No. Sources of selection, information, and confounding biases could potentially affect any study, irrespective of sample size (or power). That said, very large studies conducted by highly experienced investigators generally make every effort to address such problems in the design and analysis and would discuss these issues in their publications. Also, studies of individual-level data may have access to more information to address bias than meta-analyses or aggregate-level studies.

2) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4 (Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are generally assessing the associations between ambient ozone and specific health outcomes and are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40 and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to ozone, then should this caveat always be considered when evaluating exposure concentrations associated with these types of epidemiology studies?*

> **Response:** The two statements cited are generally correct and apply broadly to air pollution epidemiology studies, not just ozone. Most epidemiologic studies are based on measurements of ambient pollution levels, which are readily available. For some pollutants, indoor sources or penetration from outdoor sources, local variation in pollutant concentrations, time-activity patterns, etc., can be important sources of inter-individual variation, which some studies have attempted to quantify by, for example, personal monitoring, microenvironmental measurements, exposure modeling, GPS or accelerometer instruments, etc., but such studies are expensive and may be infeasible for large-scale epidemiologic studies. Since the statements queried do apply to ozone studies, I don't see than any particular caveats are needed to point out the generality of this issue.

Exposure-Response Modeling

3) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of data for some at risk groups and the potential for such groups, such as children with asthma, to*

experience lung function decrements at lower exposures than healthy adults, both models generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human exposure studies." Is assuming a lack of threshold in an exposure-response relationship a standard method for considering potential at-risk populations that may not have been characterized in an exposure-response assessment?

Response: As I pointed out in earlier rounds of questions, the exact shape of a dose-response relationship at low doses, including the existence or not of a threshold, is difficult if not impossible to determine from feasible-sized epidemiologic studies. Hence, the default analysis model generally assumes low-dose linearity (or log-linearity depending on the form of the outcome variable); see for example the classic paper by Crump, Hoel, Langley, and Peto (1976) I previously cited. This would be true for either main effects in the whole population or for effect modification in potentially sensitive subpopulations, to the extent that the necessary data on individuals are available. The question of effects below the current standard is particularly important, and especially for highly sensitive groups; to the extent that such data exist, any demonstrable low-dose associations should be considered in revising the standard, whether or not the assumption of low-dose linearity or thresholds can be tested.

4) *The EPA also notes in this section that there is a lack of information about the factors that make people more susceptible to ozone-related effects, and that the risk assessment could therefore be underestimating the risk. However, the exposure-response model used to estimate the risk of lung function decrements uses those people in the health population with a greater response to ozone than the mean response (i.e. that fraction of the people in controlled human exposure studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration for more susceptible people in the population?*

Response: This question appears to relate more to controlled human exposure studies than to epidemiologic studies but does seem to be a reasonable approach for getting a handle on inter-individual variability in susceptibility in that context. Obviously, the slope of an exposure-response relationship in the general population will underestimate risk for more sensitive individuals, or more importantly, for identifiable subgroups. Of course, there are other characteristics than lung function (e.g., genetic variants, age/gender, baseline health status, etc.) that could influence sensitivity of ozone or other pollutants. To the extent that the necessary data are available, most epidemiologic studies have reported variation across quantifiable subgroups, and given EPA's mandate to provide adequate protection to such groups as well as to the entire population should be taken into consideration in revising standards.

Questions from Dr. James Boylan

Chapter 2 – Air Quality

Not my area of expertise.

Chapter 3 – Review of the Primary Standard

- *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section 3.4.1) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard (Section 3.4.2) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what additional information needs to be included?*
- *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not, what additional information needs to be included?*

> **Response:** I found the passages that I read to be accurate and complete, to the best of my knowledge.

Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses

Not my area of expertise.

Questions from Dr. Corey Masuca

None of these are in my area of expertise.