

**Clean Air Scientific Advisory Committee (CASAC) Draft Report (01/21/2020) to Assist Meeting Deliberations
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This draft CASAC report is a work in progress, does not reflect consensus advice or recommendations, has not been reviewed or approved by the Chartered CASAC, and does not represent EPA policy.

DATE

EPA-CASAC-20-XXX

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, 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 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-member consultants and their responses are also enclosed. Major comments and recommendations are highlighted below and detailed in the consensus responses to charge questions.

Overall, the CASAC finds that 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 of evidence presented to public health. 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 ozone annual standard. Other members of CASAC question the previous Administrator's judgment that the current annual Ozone National Ambient Air Quality Standards (NAAQS) protect public health with an adequate margin of safety, while agreeing

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1 that the underlying scientific evidence and data have not greatly changed since the previous review. The
2 CASAC also finds, in agreement with the EPA, that the available evidence does not reasonably call into
3 question the adequacy of the current secondary ozone standards and concurs that they should be
4 retained.

5
6 On overarching process issues, the CASAC strongly recommends that the EPA consider restoring a
7 traditional interactive discussion process in which the CASAC can interact directly with external expert
8 panels, while also keeping the option of obtaining written responses from external experts to specific
9 questions. The CASAC strongly recommends that the EPA work with experts in causal analysis and
10 analytics methodology from outside the NAAQS community (e.g., using the National Academies Board
11 on Mathematical Sciences and Analytics) to improve the soundness and clarity of causal conclusions
12 throughout the ISA and PA. The CASAC recommends that it be given an opportunity to review a second
13 draft of the Ozone PA (with an updated REA) after the final ISA for ozone is released.

14
15 Turning to specific comments on chapters in the Draft Ozone PA, the CASAC finds that Chapter 1 gives
16 a clear, although brief, discussion of legislative background and history that provides useful context for
17 the review. For the final PA, the CASAC recommends that the EPA consider adding a discussion of the
18 exceptional nature of the current CASAC and NAAQS review process. This could include: (a) further
19 details of Administrator Pruitt's "Back to Basics" memorandum; (b) proceeding without an Ozone
20 Review Panel and streamlining the review process to promote timely advice; (c) appointing a pool of
21 non-member consultants to expand the expertise and fields of knowledge used to inform the CASAC's
22 review; and (d) the CASAC's explicit emphasis on associational bases versus biological and other bases
23 for causal conclusions, and reexamination of frameworks used in previous reviews. The CASAC
24 recommends several measures to more fully realize the Draft Ozone PA's stated goals of serving as a
25 source of policy-relevant information, being understandable to a broad audience, and facilitating the
26 CASAC's advice to the Agency and recommendations to the Administrator.

27
28 The CASAC finds the information in Chapter 2 to be clearly presented and useful as context for the
29 review, but recommends adding discussions of how precursors contribute to ozone formation, and their
30 relative importance, as well as differences in seasonality and trends within and between different regions
31 of the United States. The treatment of ozone exposures related to wildfires and exceptional events
32 should be expanded and clarified.

33
34 The CASAC has several specific recommendations, detailed in the attached report, for improving the
35 accuracy, balance, comprehensiveness, and soundness of the material in Chapter 3. The CASAC
36 recommends that the final ISA should provide a more balanced report of relevant epidemiology, as
37 discussed further for the Draft Ozone ISA; causality determinations for metabolic effects should be
38 updated to reflect the Final Ozone ISA; that FEV₁ decrements are not the only relevant health effect
39 from ozone exposure should be more fully discussed, along with its implications for interpretation and
40 application of the risk assessment results; and lack of empirical validation for risk modeling assumptions
41 and predictions should be acknowledged and its implications for uncertainty about public health effects
42 of changes in ozone exposures should be discussed. The CASAC recommends that a thorough

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1 quantitative uncertainty and variability analysis should be added and its implications for policy-relevant
2 conclusions discussed.

3
4 The CASAC commends the EPA for the thorough discussion and rationale for the secondary standard in
5 Chapter 4, and agrees with the EPA that the current secondary standard for ozone should be retained.
6 However, the CASAC recommends that the Draft Ozone PA should more thoroughly address effects of
7 ozone on climate change by providing quantitative estimates and uncertainty bands for effects of ozone
8 on global warming and the consequence for economic and welfare effects on the United States.

9
10 The CASAC appreciates the opportunity to provide advice on the Draft Ozone PA and looks forward to
11 the agency's response.

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15 Sincerely,

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20 Dr. Louis Anthony Cox, Jr., Chair
21 Clean Air Scientific Advisory Committee
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32 Enclosures

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NOTICE

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2
3 This report has been written as part of the activities of the EPA's Clean Air Scientific Advisory
4 Committee (CASAC), a federal advisory committee independently chartered to provide extramural
5 scientific information and advice to the Administrator and other officials of the EPA. The CASAC
6 provides balanced, expert assessment of scientific matters related to issues and problems facing the
7 agency. This report has not been reviewed for approval by the agency and, hence, the contents of this
8 report do not represent the views and policies of the EPA, nor of other agencies within the Executive
9 Branch of the federal government. In addition, any mention of trade names or commercial products does
10 not constitute a recommendation for use. The CASAC reports are posted on the EPA website at:
11 <http://www.epa.gov/casac>.

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**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 REA) 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-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, as well as external experts and many public commentators, found that the meanings of the causal determination categories are unclear. Current causal determinations, and conclusions stated using them, are ambiguous because they do not distinguish between essentially different concepts (such as necessary cause, sufficient cause, contributing cause, and other causal concepts). These distinctions are important for policy purposes. Yet, discussions with the EPA during the public meetings and written comments from non-member consultants show that it is demonstrably unclear, even to expert readers, what claims made using the current causal determination categories mean; their scientific truth cannot be determined due to this ambiguity. The CASAC therefore strongly recommends that the EPA work with experts in causal analysis and methodology from outside the NAAQS community, perhaps using the National Academies (e.g., the Board on Mathematical Sciences and Analytics), to critically review and improve the logical and conceptual foundations for its

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1 causal analyses and the clarity with which its causal conclusions are expressed and communicated
2 throughout the NAAQS review process and in the ISA and PA.

3
4 Response to Charge Question

5
6 *To what extent does the CASAC find that the information in Chapter 1 is clearly presented and that it*
7 *provides useful context for the review?*

8
9 The discussions of legislative background and history are clearly, although briefly, presented. They
10 provide useful context for the review.

11
12 For the final PA, the CASAC recommends that the EPA consider adding a discussion of the exceptional
13 nature of the current CASAC and NAAQS review process. Relevant background on changes in
14 processes and procedures could include: (a) further details of Administrator Pruitt’s “Back to Basics”
15 memorandum (adding to the discussion on p. 1-12); (b) proceeding without an Ozone Review Panel and
16 streamlining the review process to promote timely advice; (c) appointment of a pool of non-member
17 consultants to expand the expertise and fields of knowledge used to inform the CASAC’s review; and
18 (d) the CASAC’s explicit emphasis on associational bases vs. biological and other bases for causal
19 conclusions, and reexamination of frameworks used in previous reviews.

20
21 Relevant background on methodological changes in the current CASAC’s scientific and technical
22 approach in this review cycle could be provided in a separate section. These include the following:

23
24 (1) Drawing and preserving key conceptual distinctions between:

- 25 a. Statistical association vs. biological (mechanistic) concepts of causation;
26 b. Verifiable scientific conclusions vs. expert judgments as bases for forming and
27 communicating policy-relevant causal conclusions.

28 The CASAC recommends that these methodological issues, together with improved definitions
29 and methods for drawing and expressing causal inferences about health risks that can be
30 prevented by reducing exposures, should made high-priority topics for future research and
31 methodology development. As stated above, the CASAC recommends that the EPA involve the
32 National Academies in a careful examination of these issues.

33
34 (2) Emphasis on more effective integration of information from animal toxicology and controlled
35 human exposure studies to:

- 36 a. Elucidate and validate potential (i.e., hypothesized) causal biophysical mechanisms
37 underlying epidemiologically suggested health risks; and
38 b. Better characterize causal biological concentration-response (C-R) functions for pulmonary
39 inflammation and other physiological responses in response to inhaled ozone.

40
41 The stated intentions for the Draft Ozone PA presented in Chapter 1 include “to serve as a source of
42 policy-relevant information;” “to be understandable to a broad audience;” and “to facilitate advice to the

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Agency and recommendations to the Administrator” from the CASAC. The CASAC recommends that these intentions be more fully realized in the Draft 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 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.
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. The final PA should use validated causal C-R functions to understand and interpret observed and predicted effects of alternative policy choices.
4. *Discuss in more detail the health and policy implications of causal biological mechanisms of inflammation-related health effects in general and sensitive populations* preventable by reducing current ozone levels, including roles of inflammation in mediating persistent 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 ISA’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 (O₃ and Photochemical Oxidants in the Atmosphere) should discuss how the precursor emissions listed in this section, oxides of nitrogen (NO_x), volatile organic compounds (VOCs), carbon monoxide (CO), and methane (CH₄), 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 local (both urban and rural) ozone formation and ozone formation in the remote troposphere. Also, the relative importance of NO_x 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 O₃ Precursors) presents estimated national values for 2014 National Emissions Inventory (NEI) emissions. However, there is no detailed discussion on the

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1 uncertainty associated with each pollutant or source sector. Some pollutants and sectors will be much
2 more uncertain than others. For example, NO_x emissions from electric generating units (EGUs) have
3 low uncertainty since they are typically captured by hourly continuous emissions modeling (CEMs). On
4 the other hand, other source sectors and pollutants may be highly uncertain. The uncertainties in the
5 emissions inventory (magnitude, spatial allocation, and temporal allocation) should be discussed for
6 each pollutant and source sector. In addition, it would be helpful to add national maps containing
7 county-level emissions for NO_x, VOCs, CO, and CH₄ to show the variability across the country. It is not
8 clear if CH₄ is included in the VOC emissions or not. The text should clearly state if CH₄ is included or
9 excluded from the VOC emissions discussed in this chapter.

10
11 Section 2.4 (Ozone in Ambient Air) should include a discussion on ozone precursor trends in addition to
12 ozone trends. Specifically, trends in NO_x, VOCs, and CO measurements from national monitoring
13 networks (AQS, near-road, NCore, and PAMS) should be included and discussed.

14
15 It is stated on page 2-19, “B shows the seasonal pattern for an urban site in Baton Rouge, LA.
16 Throughout the southeastern U.S., the highest O₃ concentrations are often observed in April and May
17 due to the onset of warm temperatures combined with abundant emissions of biogenic VOCs at the start
18 of the growing season. This is often followed by lower concentrations during the summer months, which
19 is associated with high humidity levels that tend to suppress O₃ formation.” Although this statement
20 might be true for Baton Rouge, it does not apply to the entire southeastern United States. In addition, a
21 reference should be provided to support the statement that high humidity levels suppress O₃ formation.

22
23 EPA’s 2016 Exceptional Events Rule allows certain ozone measurements due to natural events to be
24 excluded from the official design values when compared to the NAAQS. In some cases, identical
25 exceptional events can be treated differently in one location vs. another based on how close the area is to
26 the standard. In both locations, people are impacted by adverse health effects, but the data is removed in
27 one location and not the other. The Draft Ozone PA should discuss how exceptional events are
28 accounted for in the policy assessment.

29
30 Section 2.5 (Background O₃) describes the EPA’s use of the Community Multiscale Air Quality
31 (CMAQ) chemical transport model with the zero-out approach to estimate U.S. background,
32 international, and natural contributions. Figures 2-22, 2-23, and 2-24 should add a 100% line. The EPA
33 should add explanations for values over the 100% line. The caption in Figure 2-26 is incorrect. The
34 figures and tables containing U.S. Background (USB) contribution on the average of the top 10
35 predicted O₃ days and the 4th highest O₃ days are very useful and relevant to policy decisions. These
36 values should be compared to previous work by Jaffe et al. (2018) and Parrish et al. (2017, 2019). In
37 Appendix 2B, the scale used in Figure 2B-15 should be reduced from 100% to a lower value to allow the
38 reader to see the differences between monitoring sites.

39
40 The EPA should consider extending the Photochemical Assessment Monitoring Stations (PAMS)
41 monitoring season from 3 months (June, July, August) to 6 months (mid-April, May, June, July, August,
42 September, mid-October) in ozone nonattainment areas since peak ozone concentrations have been

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1 shifting from summer to late spring and early fall. Ozone exceedances that occur in the late spring and
2 early fall may be impacted by different VOC species than ozone exceedances that occur in the summer.
3
4

5 **Chapter 3 – Review of the Primary Standard**
6

7 *What are the CASAC views on the approach described in Chapter 3 to considering the health effects*
8 *evidence and the risk assessment in order to inform preliminary conclusions on the primary standard?*
9 *What are the CASAC views regarding the key considerations for the preliminary conclusions on the*
10 *current primary standard?*
11

12 **Air Quality**
13

14 The EPA states in section 3.1.2.2 that “Analyses described in detail in the [Health Risk and Exposure
15 Assessment] HREA suggested that reductions in O₃ precursors emissions in order to meet a standard
16 with an 8-hour averaging time, coupled with the appropriate form and level, would be expected to
17 reduce O₃ concentrations in terms of the metrics reported in epidemiologic studies to be associated with
18 respiratory morbidity and mortality (80 FR 65348, October 26, 2015).” However, multiple ozone
19 chemistry analyses (e.g., Downey et al., 2015; Simon et al., 2012) have demonstrated that peak and
20 lowest daily ozone concentrations typically move in the same direction (due to the NO_x disbenefit
21 aspect of ozone chemistry). An example is provided in Figure 1. The non-member consultants generally
22 agreed that decreasing peak ozone concentrations will not consistently decrease the mean ozone
23 concentrations and therefore is not necessarily expected to improve the metrics associated with
24 respiratory mortality and morbidity in epidemiology studies. The CASAC recommends that the EPA
25 reconsider their statement.
26

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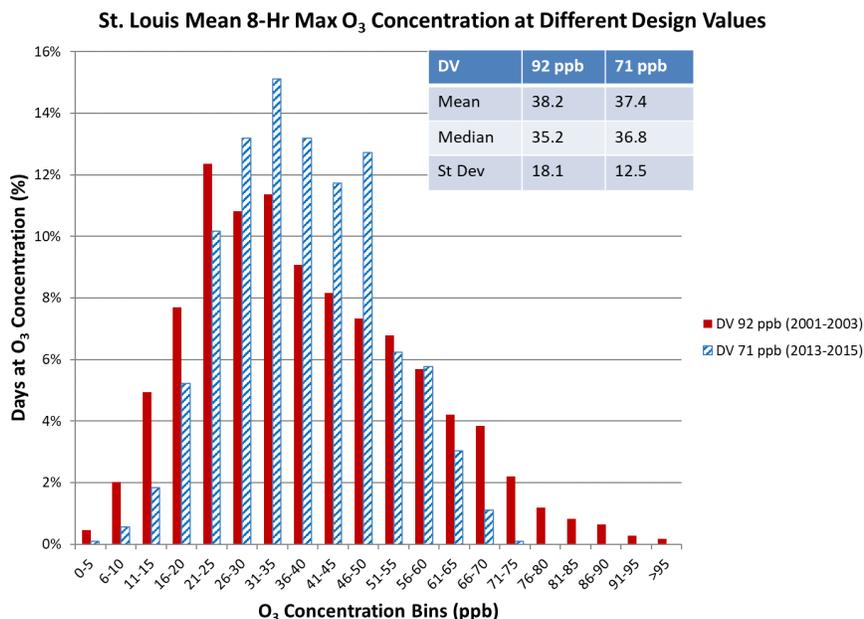


Figure 1. Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV – design value. Data from EPA’s Air Quality System and analyzed similarly to the analyses in Lange (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 O₃ 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 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 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.

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1 Fully Justified Conclusions
2

3 Chapter 3 requires some editing to ensure that stated conclusions are fully supported.
4

5 Section 3.3.1.2 (Other Effects) does not adequately explain why the evidence for metabolic effects is
6 *likely causal*. The data are mostly from animal studies with high exposure levels. There is limited
7 concordance with human epidemiology studies, and some of the evidence is contradictory. Similar
8 limitations hold for long-term exposure and metabolic effects. The CASAC recommended in comments
9 on the Draft Ozone ISA that the EPA reconsider the causality determination between short-term and
10 long-term ozone exposure and metabolic effects. For the Ozone PA, the CASAC recommends that the
11 causality determination for metabolic effects be updated to reflect the Final Ozone ISA.
12

13 Additional Policy-Relevant Information
14

15 In Section 3.3.2, it would be helpful to add a discussion of what fraction of the population (particularly
16 at-risk populations if possible) is expected to spend 6.6 hours or more outdoors at moderate exertion.
17 This information would aid decision makers in comparing exposure likelihood to the primary controlled
18 human exposure (CHE) studies.
19

20 Section 3.3.2 (Public Health Implications and At-Risk Populations) lacks adequate discussion about
21 greater susceptibility for minority and/or lower socioeconomic status (SES) populations. More
22 information about these populations should be included.
23

24 In the risk assessment conducted for the 2015 Ozone NAAQS, the EPA included risk estimates for
25 occupational workers. Those risk estimates could be discussed in this document to address that
26 potentially at-risk population.
27

28 Study Limitations
29

30 The CASAC commends the EPA for its important caveats in Section 3.3.3, stating that “We have also
31 considered what may be indicated by the epidemiologic studies regarding exposure concentrations
32 associated with health effects, and particularly by such concentrations that might occur in locations
33 when the current standard is met. In so doing, however, we recognize that these studies are generally
34 focused on investigating the existence of a relationship between O₃ occurring in ambient air and specific
35 health outcomes, and not on detailing the specific exposure circumstances eliciting such effects... These
36 studies generally do not measure personal exposures of the study population or track individuals in the
37 population with a defined exposure to O₃ alone. Notwithstanding this, we have considered the
38 epidemiologic studies identified in the draft ISA as to what they might indicate regarding O₃ exposure
39 concentrations in this regard.”
40
41
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1 Clarity of Presentation
2

3 To ensure that data and analyses are clearly reported, Section 3.2 (General Approach and Key Issues in
4 this Review) should clarify the purpose of the risk assessment in the policy assessment evaluation, and
5 how it is used in the decision-making process.
6

7 In Section 3.4.2 (Population Exposure and Risk Estimates for Air Quality Just Meeting the Current
8 Standard) and elsewhere, population exposure estimates (i.e., the estimates of percent of the population
9 exposed to certain concentrations of ozone) are referred to as risk estimates. Definitions of risk and
10 exposure should be clarified.
11

12 The Draft Ozone PA presents quite different risk estimates produced by the McDonnell Stewart Smith
13 model (MSS) and exposure-response (E-R) models. These are discussed at length in Appendix 3D, with
14 an in-depth justification of the choice of the E-R model risk results over the MSS results. The EPA
15 should add more of the information from Appendix 3D to the main text.
16

17 The EPA states that “The limited evidence that informs our understanding of potential risk to people
18 with asthma is uncertain but indicates the potential for them to experience greater effects or have lesser
19 reserve to protect against such effects than other population groups under similar exposure
20 circumstances, as summarized in Section 3.3.4 above.” But the limited evidence does not indicate the
21 potential for people with asthma to experience greater effects, although they may have less reserve.
22 These two aspects need to be distinguished and discussed separately. In quantitative risk assessment,
23 greater effects correspond to a steeper E-R response or a lower threshold (although there is little data to
24 suggest that this is the case) whereas diminished reserve corresponds to a lower adverse effect threshold.
25

26 The CASAC recommends that EPA consider adding a summary to Section 3.4.5 about the percent of
27 children with asthma estimated to experience a 10% FEV₁ decrement, with a short discussion about the
28 adversity of those changes in lung function.
29

30 Focus on Lung Function Decrements in the Risk Analysis
31

32 The CASAC has the following concerns about the approach taken for the ozone risk assessments
33 presented in the Draft Ozone PA. The essentially exclusive use of lung function decrements in assessing
34 ozone risk does not adequately consider other respiratory effects that are likely to be important in people
35 with respiratory diseases such as asthma. The following summary points are addressed below: 1)
36 Asthma is a complex disease, with several important features beyond airflow limitation; 2) Many of the
37 key features of asthma pathophysiology can be affected by exposure to ozone; 3) The risk assessments
38 are based almost exclusively on studies in healthy adults and make unverified assumptions about ozone
39 health effects in children with asthma.
40

- 41 1. Asthma is a complex disease (Fanta, 2009). It involves airflow limitation, airway inflammation,
42 and nonspecific airways hyperresponsiveness. Injury to, and increased permeability of, the
43 airway epithelium is an increasingly recognized feature of the disease. Remodeling of the

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1 airways is also part of asthma, with thickening of the submucosal basement membrane
2 consistently seen in lung biopsies of people with asthma, even in those with normal pulmonary
3 function.
4

5 Many people with asthma have normal lung function and are asymptomatic at baseline, but other
6 features of the disease, including airway inflammation and airways hyperresponsiveness, persist
7 even when they are in remission from the symptoms of the disease. Most children with asthma
8 are able to be active and exercise outdoors. They develop problems when something triggers an
9 exacerbation, such as exposure to an allergen to which they are sensitized, a respiratory
10 infection, or air pollutants, among others. Arguably the most important potential adverse effect
11 of acute ozone exposure in a child with asthma is not whether it causes a transient decrement in
12 lung function, but whether it causes an asthma exacerbation.
13

- 14 2. Ozone has respiratory effects beyond its well-described effects on lung function. It increases
15 airway inflammation, a key component in the pathophysiology of asthma. Eosinophilic
16 inflammation is particularly important in allergic asthmatics, and we know from clinical studies
17 that airway eosinophilia is increased in response to ozone exposure in asthmatics (Peden et al.,
18 1997), especially when ozone is combined with an allergen challenge (Vagaggini et al., 2002).
19 Ozone increases non-specific airways hyperresponsiveness in clinical studies. Ozone exposure
20 causes airway epithelial injury and increases airway epithelial permeability, both cardinal
21 features in asthma pathophysiology. This increases the potential for materials deposited in the
22 distal airways, such as particles or allergens, to reach the lung interstitium and vascular space.
23 These effects beyond lung function decrements likely contribute to the risk of an asthma
24 exacerbation. Yet they are not captured or considered in the Draft Ozone PA's risk analysis.
25

26 EPA's current approach minimizes the full spectrum of potential ozone airway effects. The focus
27 in the risk assessment is solely on FEV₁, because that database is robust. But we know from
28 other studies that the FEV₁ response and the airway inflammatory response occur via different
29 mechanisms (Torres et al., 1997; Frampton et al., 1997; Balmes et al., 1996), and some people
30 are more prone to one of these effects than the other. This means that there are individuals who
31 will experience increases in airway inflammation without lung function decrements, or
32 symptoms. The absence of symptoms could result in a failure of the individual to limit exposure,
33 thereby further worsening the airway inflammatory effect of the exposure.
34

35 It is reasonable to expect that, in people with asthma, any increase in airway inflammation is an
36 adverse effect, with the potential to increase the risk for an asthma exacerbation. Repeated
37 episodes of airway inflammation may enhance airway remodeling, which occurs in asthma, and
38 leads to irreversible reductions in lung function.
39

- 40 3. The Draft Ozone PA makes the following assumptions:
41 a. *Lung function decrements in response to 7-8 hour exposures near 70 ppb are the same in*
42 *children with asthma as they are in healthy adults.* The clinical data in people with mild to
43 moderate asthma, exposed at higher concentrations than those directly relevant to the

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1 standard, suggest that people with asthma do not have markedly increased FEV₁ declines
2 compared with healthy subjects. But it is inappropriate to assume that this extends to lower
3 concentrations, or to people with more severe disease. People with asthma do appear to
4 experience greater effects on measures of airway obstruction, including airways resistance
5 testing. This is briefly reviewed in the Draft Ozone ISA, but not considered in the risk
6 assessment. None of the low-concentration, 6- to 7-hr studies listed in Tables 3A-1 and 3A-2
7 included people with asthma. Very few clinical studies have included severe or even
8 moderate asthma, let alone children with asthma, and none have included people with
9 unstable asthma or those prone to exacerbations. This is a key knowledge gap and raises
10 legitimate questions about whether the current standard provides an adequate margin of
11 safety for people with asthma.

- 12 b. *Absence of symptoms means less adversity.* The Draft Ozone PA seems to suggest that lung
13 function decrements in the absence of symptoms do not represent an adverse health effect.
14 But this should not apply to children with asthma, for the reasons discussed above, and as
15 addressed more fully in the European Respiratory Society/American Thoracic Society
16 statement on adverse health effects of air pollution (Thurston et al., 2017).
- 17 c. *Lung function and other respiratory effects are rapidly reversible in asthmatic children,*
18 *similar to healthy adults.* The time course of the pulmonary function response is well-
19 established in healthy adults, but less well in children, and especially in children with asthma.
20 There are no data on the persistence of respiratory effects in people with asthma following
21 low-concentration, more prolonged exposures.

22
23 The EPA should further address these points in the Draft Ozone PA, discuss how FEV₁ decrements are
24 not the only relevant health effect from ozone exposure, and explicitly consider how these points impact
25 the interpretation and application of the risk assessment results.

26
27 Risk Models

28
29 Chapter 3 and its supporting appendices predict risks using models and assumptions that have not been
30 validated for predicting how changes in ozone affect public health risks. They omit important caveats
31 similar to those provided in the EPA's 2014 Ozone HREA. These included the following for the 2012
32 MSS model (emphases added):

- 33 • “Clearly the **intra-individual variability**... in the MSS model is a key parameter and is
34 influential in predicting the proportions of the population with FEV₁ decrements >10 and 15%.
35 **The assumption that the distribution of this term is Gaussian is convenient for fitting the**
36 **model, but is not accurate.** The extent to which this mis-specification affects the estimates of
37 the parameters of the MSS model and its predictions is not clear.”
- 38 • “Although **the model does not have good predictive ability for individuals** (psuedo-R² 0.28),
39 it does better at predicting the proportion of individuals with FEV₁ decrements 10, 15, and 20%
40 (psuedo-R²s of 0.78, 0.74, 0.68) (McDonnell et al., 2012). The clinical studies that these model
41 estimates are based on were conducted with young adult volunteers rather than randomly
42 selected individuals, **so it may be that selection bias has influenced the model parameter**
43 **estimates.** The parameter estimates are not very precise, partly as the result of correlations

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1 between the parameter estimates....The MSS model is also sensitive to the exposure
2 concentrations, but we have not quantified that sensitivity....**We are unable to properly**
3 **estimate the true sensitivities or quantitatively assess the uncertainty of the MSS**
4 **model**....As discussed in Section 6.5.3 below, there are uncertainties in extrapolating the MSS
5 model down to age 5 from the age range of 18 to 35 to which the model was fit....[T]he
6 uncertainty of the extension to children of the MSS model could be substantial.” Section 6.5.7
7 adds that “EPA staff have identified key sources of uncertainty with respect to the lung function
8 risk estimates. These are: the physiological model in APEX for ventilation rates, the O₃
9 exposures estimated by APEX, the MSS model applied to ages 18 to 35, and extrapolation of the
10 MSS model to children ages 5 to 18....**At this time we do not have quantitative estimates of**
11 **uncertainty for any of these.**”
12

13 The Draft Ozone PA does state that “We are using this model to estimate lung function decrements for
14 people ages 5 and older. However, this model was developed using only data from individuals aged 18
15 to 35 and the age adjustment term [$\beta_1 + \beta_2 (\text{Age}_{ijk} - 23.8)$] in the numerator of Equation 3D-13 is not
16 appropriate for all ages.” However, the fact that the model predictions are based on assumptions that are
17 unlikely to be accurate (e.g., that the parameter alpha 2 in Table 3D-21 quadruples on one’s 18th
18 birthday) and that the models and their predictions have not been empirically validated or verified
19 should be emphasized. In effect, the Draft Ozone PA selects some specific parametric models and uses
20 them to make risk predictions, but the validity of the models and their predictions is unknown. The final
21 PA should discuss the internal and external validity of the risk models and their predictions and should
22 present the results of empirical validation tests for the risk models and predictions.
23

24 Quantitative Uncertainty Analysis

25
26 The EPA does not provide uncertainty bounds on their exposure or risk estimates. The ranges presented
27 represent variability between cities, not uncertainty. There are many ways that some measure of
28 uncertainty can be accounted for in these estimates, some of which are discussed and presented in
29 Appendix 3 – these should be included in the main text to provide information for decision making. For
30 example, on page 3D-145, the EPA references the work of Glasgow and Smith (2017), who provide a
31 method for quantitative uncertainty evaluation. There is also an upper bound estimate of the E-R
32 function that is presented in Table 3D-64 – if there was an upper and lower bound function provided,
33 then those could simply be used for some quantification of uncertainty.
34

35 The EPA discusses uncertainties with air quality analysis in Section 3.4.4 (Key Uncertainties) as well as
36 the ways in which they have tried to reduce this uncertainty. However, this type of uncertainty is a prime
37 candidate for a quantitative uncertainty analysis because there are estimates on the uncertainties
38 associated with the air quality estimates.
39

40 Appendices 3C and 3D

41
42 The more detailed discussion on selection of study areas should be moved from Section 3D.2.1 to
43 Section 3C.2 since Appendix 3C is presented prior Appendix 3D. It appears that Sacramento (2017

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1 design value = 86 ppb) does not meet the second selection criteria listed on page 3D-14, “Combined
2 statistical area (CSA)/metropolitan statistical area (MSA) ambient air 24 monitor design values are
3 between 60-80 ppb, thus having minimal adjustment needed to just meet the current 8-hr O₃ NAAQS”.
4 A reason for selecting this study area should be added to the document.
5

6 It appears that the CAMx chemical transport model was only run with 2016 meteorology while the
7 APEX exposure model was run using 2015-2017 meteorological data. The document should explain
8 how these two models were combined to generate 2015-2017 exposures.
9

10 A comparison of 2016 emissions used in the CAMx model (Table 3C-4) to the 2014 NEI emissions
11 (Figure 2-1) show similar emissions for CO and VOCs (after adjusting for year-specific biogenic
12 emissions). However, the anthropogenic NO_x emissions in 2016 are 20% lower than the anthropogenic
13 NO_x emissions in 2014. This large difference should be explained.
14

15 The EPA performed an ozone model performance evaluation (MPE) for each study area. However,
16 additional explanation is needed to describe the time series plots shown on pages 3C-34 – 3C-61. It
17 appears that the measured MDA8 is averaged for all monitors in an area and compared to the modeled
18 MDA8 average for all monitors in the area. The document should explain how the modeled MDA8
19 average is calculated when observations are missing. For example, do the corresponding model results
20 get removed or do they remain in the average? Also, it appears that the “# of sites” included in the top
21 right corner of each plot includes both CSA and “buffer” sites. It would be more appropriate to only
22 include CSA sites since this would better match with the study areas used in the exposure modeling. The
23 “# of sites” shown in Figure 3C-25 for January is “14”. However, Georgia only has two year-round
24 monitors in the state. For each study area and season, it would be useful to plot all hourly observed and
25 modeled concentrations in a single 24-hour diurnal plot with means and standard deviations (similar plot
26 as Figure 3C-67).
27

28 The document should include the number of monitors used in each model performance summary table
29 contained on pages 3C-31 – 3C-59. It is unclear if the “buffer” sites are included along with the CSA
30 sites. Again, it would be most appropriate to only include CSA sites.
31

32 In addition to the ozone MPE, it would be useful to perform an MPE for the ozone precursors (NO_x and
33 VOCs). If the precursor concentrations don’t match the observations, the HDDM sensitivity results may
34 not be accurate even if the ozone concentrations match observations.
35

36 Figures 3C-67 and 3C-75 for Atlanta are both missing the “75 ppb” ozone distributions. Although NO_x
37 emissions were not adjusted in Atlanta for the 75 ppb scenario, the modeling results for the 75 ppb
38 scenario should still be included.
39

40 Section 3C.5.2.2.3 should discuss why NO_x reductions alone were selected for adjusting design values.
41 In many cases, VOC reductions occur simultaneously with NO_x reductions. Also, many areas of the
42 county are equally as sensitive to VOC reductions as NO_x reductions.
43

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

3
4 The exposure and risk results from the 7 study areas that are in common with the previous ozone HREA
5 review should be compared and similarities/differences discussed in this document.

6
7 There is a figure (referenced in page 3D-91) that seems to be labeled as “0”, instead of with the figure
8 number.

9
10 P. 3D-80. For the MSS model, lung function decrements are assumed to be 0 for age >55 yrs. This
11 model does not incorporate newer data on lung function effects in healthy older subjects (Frampton et
12 al., 2017), which demonstrated lung function effects in subjects older than 55 yrs. This should be
13 acknowledged in the PA.

14
15 In the Appendices, in a number of locations, there is the statement “Error Reference Not Found!” - these
16 need to be located and fixed.

17
18 Other Notes

19
20 In section 3.3.1.1 Footnote: “As recognized in Section 3.3.1.1 above, the single newly available 6.6-hour
21 study is for subjects aged 55 years of age or older, and has a slightly lower target ventilation rate for the
22 exercise periods. The exposure concentrations were 120 ppb and 70 ppb, only the former of which
23 elicited a statistically significant FEV1 decrement in this age group of subjects (draft ISA, Appendix 3,
24 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-
25 hour exposure.

26
27 In Section 3.4.1 (Conceptual Model and Assessment Approach), p. 3-50, line 7: Rather than “assessing
28 exposure, ventilation rate, intake dose, and estimated health risk,” the CASAC suggests “estimating
29 exposure, ventilation rate, ozone intake, and health risk.”

30
31 The end of the second bullet point on page 3-51 is cut-off mid-sentence.

32
33 The last sentence of the first paragraph on page 3-82 needs to be edited - there seem to be words missing
34 or juxtaposed.

35
36 Conclusions

37
38 The CASAC agrees that the evidence newly available in this review that is relevant to setting the ozone
39 standard does not substantially differ from that of the 2015 Ozone NAAQS review. Most of the CASAC
40 agrees with the EPA that the available evidence does not call into question the adequacy of protection
41 provided by the current standard, and thus support retaining the current primary standard. Some of the
42 members of CASAC think that the current ozone primary standard does not provide an adequate margin
43 of safety in the protection of children with asthma.

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1 Future Research
2

3 *What are the CASAC views regarding the areas for additional research identified in Chapters 3 and 4?*
4 *Are there additional areas that should be highlighted?*
5

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

- 7 • PAMS monitoring information for the months of April through October in ozone nonattainment
8 areas, since peak ozone concentrations have been shifting from summer to late spring and early
9 fall. Ozone exceedances that occur in the late spring and early fall may be impacted by different
10 VOC species than ozone exceedances that occur in the summer.
- 11 • Further research into current ozone chemistry and how it may be impacted by climate change.
- 12 • Research into development of more efficient and effective control strategies for ozone reduction.
- 13 • Assessment of respiratory effects other than FEV₁ at ozone levels that are in the range of the
14 current standard, particularly endpoints such as airway hyper-responsiveness and airway
15 inflammation that are important for children with asthma.
- 16 • External validation of the FEV₁ E-R and MSS models, and validation with other FEV₁ models.
- 17 • Further research into the metabolic effects of ozone, particularly in human populations for
18 clinical health outcomes such as metabolic syndrome, diabetes, etc., as well as intermediate
19 indicators like insulin resistance; and in animal toxicology studies at concentrations closer to
20 ambient concentrations.

21
22
23 **Chapter 4 – Review of the Secondary Standard**
24

25 *What are the CASAC views on the approach described in chapter 4 to considering the evidence for*
26 *welfare effects in order to inform preliminary conclusions on the secondary standard? What are the*
27 *CASAC views regarding the key considerations for the preliminary conclusions on the current*
28 *secondary standard?*
29

30 Background on the Current Standard
31

32 The current secondary standard for ozone was set in 2015, based on the scientific and technical
33 information available at that time, as well as the Administrator's judgements regarding the available
34 welfare effects evidence, the appropriate degree of public welfare protection for the revised standard,
35 and available air quality information on seasonal cumulative exposures that may be allowed by such a
36 standard (80 FR 65292, October 26, 2015). With the 2015 decision, the Administrator revised the level
37 of the secondary standard for photochemical oxidants, including O₃ to 0.070 ppm (70 ppb) in
38 conjunction with retaining the indicator (O₃), averaging time (8 hours), and form (4th-highest annual
39 daily maximum 8-hour average concentration, averaged across three years).
40

41 The welfare effects evidence base available in the previous NAAQS review included decades of
42 extensive research on the phytotoxic effects of O₃, conducted both in and outside of the United States

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1 that documents the impacts of ozone on plants and their associated ecosystems (U.S. EPA, 1978, 1986,
2 1996, 2006, 2013).

3
4 In light of the extensive evidence base, the 2013 ISA concluded there was a causal relationship between
5 ozone and visible foliar injury, reduced vegetation growth, reduced productivity in terrestrial
6 ecosystems, reduced yield and quality of agricultural crops, and alteration of belowground
7 biogeochemical cycles. In addition, the 2013 ISA concluded there was likely to be a causal relationship
8 between O₃ and reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial
9 ecosystem water cycling, and alteration of terrestrial community composition. Further, based on the then
10 available evidence with regard to O₃ effects on climate, the 2013 Ozone ISA also found there to be a
11 causal relationship between changes in tropospheric ozone concentrations and radiative forcing, found
12 there likely to be a causal relationship between tropospheric ozone concentrations and effects on climate
13 as quantified through surface temperature response, and found the evidence to be inadequate to
14 determine if a causal relationship exists between tropospheric ozone concentrations and health and
15 welfare effects related to UV-B shielding.

16
17 The 2015 secondary standard for ozone was a public welfare policy judgment made by the
18 Administrator, which drew upon the available scientific evidence for O₃-attributable welfare effects and
19 on analyses of exposures and public welfare risks based on impacts to vegetation, ecosystems and their
20 associated services, as well as judgements about the appropriate weight to place on the range of
21 uncertainties inherent in the evidence and analyses.

22
23 Considerations Regarding Adequacy of the Prior Standard

24
25 The Administrator's conclusion in the previous NAAQS review regarding the adequacy of the
26 secondary standard that was set in 2008 (0.075 ppm, as annual 4th-highest daily maximum 8 hour
27 average concentration averaged over three consecutive years) gave primary consideration to the
28 evidence of growth affects in well-studied tree species and information in cumulative seasonal ozone
29 exposures in certain study areas. In doing so, the exposure information for Class I areas was evaluated in
30 terms of the W126 Cumulative Seasonal Exposure Index, an index recognized by the 2013 Ozone ISA
31 as a mathematical approach "for summarizing ambient air quality information in a biologically
32 meaningful form for ozone vegetation effects purposes." The EPA focused on the W126 index for this
33 purpose consistent with the evidence of the 2013 Ozone ISA and advice from the CASAC. The
34 Administrator gave particular weight to analysis with focus on exposures in Class I areas, which are
35 lands that Congress set aside for specific uses intended to provide benefits to the public welfare,
36 including lands that are to be protected so as to conserve the scenic value and the natural vegetation and
37 wildlife within such areas and to leave them unimpaired for the enjoyment of future generations. This
38 emphasis on lands afforded special government protections such as national parks and forests, wildlife
39 refuges, and wilderness areas, some of which are designated as Class I areas under the Clean Air Act,
40 was consistent with a similar emphasis in the 2008 review of the NAAQS (73 FR 16485, March 27,
41 2008).

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1 As noted across past reviews of the secondary standard for ozone, the Administrator’s judgments
2 regarding effects that are adverse to public welfare consider the intended use of the ecological receptors,
3 resources, and ecosystems affected. Thus, in the previous NAAQS review, the Administrator utilized the
4 median Relative Biomass Loss (RBL) estimate for the studied species as a quantitative tool within a
5 larger framework of considerations pertaining to the public welfare significance of O₃ effects. The
6 Administrator recognized such considerations to include effects that are associated with effects on
7 growth and that the 2013 Ozone ISA determined to be causally or likely causally related to ozone and
8 ambient air, yet for which there are greater uncertainties affecting estimates of impacts on public
9 welfare. These other effects included reduced productivity in terrestrial ecosystems, reduced carbon
10 sequestration in terrestrial ecosystems, alteration of terrestrial community composition, alteration of
11 below ground biogeochemical cycles, and alteration of terrestrial ecosystem water cycles. The
12 Administrator, in considering the revised lower standard, noted that a revised standard would provide
13 increased protection for other growth-related effects, including for relative yield loss (RYL) of crops,
14 reduced carbon storage and for types of effects for which it is more difficult to determine public welfare
15 significance, as well as for other welfare effects of ozone, such as visible foliar injury (80 FR 65390,
16 October 26, 2015).

17
18 In reaching a conclusion in the amount of public welfare protection from the presence of ozone in
19 ambient air that is appropriate to be afforded by a revised secondary standard, the Administrator gave
20 particular consideration to the following:

- 21
- 22 1. The nature and degree of effects of O₃ on vegetation;
- 23 2. The strength and limitations of the available and relevant information;
- 24 3. Comments from the public on the Administrator’s proposed decision; and
- 25 4. The CASAC reviews regarding the strength of the evidence and its adequacy to inform
26 judgements on public welfare protection.

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

30
31 Does the Current Evidence Alter Conclusions from the Last Review Regarding the Nature of
32 Welfare Effects Attributable to O₃ in Ambient Air?

33
34 The evidence newly available in this current NAAQS review supports, sharpens, and expands on the
35 conclusions reached in the previous NAAQS review. Consistent with the evidence in the last
36 NAAQS Review, the currently available evidence describes an array of ozone effects on vegetation
37 and related ecosystem effects as well as the role of ozone in radiative forcing and effects on
38 temperature, precipitation, and related climate variables. Evidence newly available in this review
39 augments more limited previously available evidence related to insect interaction with vegetation,
40 contributing to conclusions regarding ozone effects on plant-insect signaling and on insect
41 herbivores. Thus, the conclusions reached by the EPA in the last NAAQS review are supported by
42 the current evidence base and conclusions are reached in a few new areas based on the now

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1 expanded evidence. The current Draft Ozone PA details of effects of ozone on vegetation and
2 ecosystem processes are reviewed in detail and updated with newly available evidence.

3
4 Public Welfare Implications

5
6 The public welfare implications of the evidence regarding ozone welfare effects are dependent on
7 the type and severity of the effects, as well as the extent of the effect at a particular biological or
8 ecological level of organization. In the Draft Ozone PA, the EPA discusses such factors in light of
9 judgements and conclusions made in prior reviews regarding effects on the public welfare. As
10 provided in Section 109(b)(2) of the Clean Air Act, the secondary standard is to “specify a level of
11 air quality the attainment and maintenance of which in the judgement of the Administrator...is
12 requisite to protect the public welfare from any known or anticipated adverse effects associated with
13 the presence of such air pollutant in the ambient air.” The secondary standard is not meant to protect
14 against all known or anticipated ozone related welfare effects, but rather those that are judged to be
15 adverse to the public welfare in a bright line determination of adversity it is not required in judging
16 what is requisite. Thus, the level of protection from known or anticipated adverse effects to public
17 welfare that is requisite for the secondary standard is a public welfare policy judgement to be made
18 by the Administrator.

19
20 Is There Information Newly Available in this Review Relevant to Consideration of the Public
21 Welfare Implications of Ozone Related Welfare Effects?

22
23 The categories of effects identified in the Clean Air Act to be included among welfare effects are
24 quite diverse and, among these categories, any single category includes many different types of
25 effects that are of broadly varying specificity and level of resolution. For instance, effects on
26 vegetation is a category identified in the Clean Air Act Section 302(h), and the Draft Ozone ISA
27 recognized numerous vegetation related effects of ozone at the organism, population, community,
28 and ecosystem level. In the decisions to revise the secondary standard in the last two reviews (2008,
29 2015) the Administrator recognized that by providing protection based on consideration of effects in
30 natural ecosystems in areas afforded special protection, the revised secondary standard would also
31 “provide a level of protection for other vegetation that is used by the public and potentially affected
32 by ozone including timber, produce grown for consumption and horticultural plants used for
33 landscaping” (80 FR 65403, October 26, 2015). The EPA provides in the Draft Ozone PA, Figure 4-
34 2 (Potential effects of O₃ on the public welfare), which does an excellent job at summarizing the
35 potential effects of causal or likely to be causal impact of ozone on vegetation at the organism,
36 population, community, and ecosystems levels.

37
38 Exposures Associated with Effects

39
40 The types of effects identified in Figure 4-2 of the Draft Ozone PA vary widely with regard to the
41 extent and level of detail of the available information that describes the ozone exposure
42 circumstances that may elicit them. Therefore, EPA organized a section in the Draft Ozone PA to
43 address first, effects of ozone exposure on growth and yield effects, a category of effects for which

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1 information on exposure metrics and E-R relationships is most advanced. In addition, the EPA
2 discusses the current information available regarding exposure metrics and relationships between
3 exposure and the occurrence and severity of visible foliar injury.
4

5 Growth Related Effects
6

7 The longstanding body of vegetation effects evidence includes a wealth of information on
8 aspects of ozone exposure that are important in influencing effects on plant growth and yield. A
9 variety of factors have been investigated, including concentration, time of day, respite time,
10 frequency of peak occurrence, plant phenology, predisposition, etc. In the last several reviews,
11 based on the then available evidence, as well as advice from the CASAC, the EPA has focused
12 on the use of cumulative, seasonal concentration-weighted index for considering the growth-
13 related effects evidence and in quantitative exposure analyses for purposes of reaching
14 conclusions on the Secondary Standard. More specifically, the EPA used the W126-based
15 cumulative, seasonal metric. This metric, commonly called the W126 Index, is a non-threshold
16 approach described as the sigmoidally weighted sum of all hourly ozone concentrations observed
17 during a specified daily and seasonal time window, where each hourly ozone concentration is
18 given a weight that increased from 0-1 within increasing concentration. The most well-studied
19 data sets in this regard are those for 11 tree species seedlings and ten crops referenced and
20 described by Lee and Hogsett (1996) and Hogsett et al. (1997). These datasets include: 1) for
21 growth effects on seedlings of a set of tree species, and 2) for quality and yield effects of a set of
22 crops. These datasets, which include growth and yield response information across a range of
23 multiple seasonal cumulative exposures, were used to develop robust, quantitative, E-R functions
24 for reduced growth (RBL). In seedlings of the tree species and E-R functions for RYL for a set
25 of common crops, the EPA's conclusions regarding exposure levels of ozone associated with
26 vegetation related effects at the time of the last review were based primarily on these established
27 E-R functions. The Draft Ozone ISA concludes that "the cumulative exposure indices, including
28 the W126 Index, "are the best available approach for studying the effects of ozone exposure on
29 the vegetation in the U.S." Accordingly, in this review, the EPA as in the last two reviews used
30 the seasonal W126-based cumulative, concentration-weighted metric for consideration of the
31 effects evidence in quantitative exposure analyses, particularly related to growth effects, which
32 appears reasonable and scientifically sound. This information for the tree species, in combination
33 with air quality analysis was a key consideration in the 2015 EPA decision on the level for the
34 revised secondary standard (80 FR 65292, October 26, 2015).
35

36 Other Effects
37

38 With regard to climate-related effects, including radiative forcing, the newly available evidence
39 in this review does not provide more detailed quantitative information regarding ozone
40 concentrations at the national scale. Although ozone continues to be recognized as having a
41 causal relationship with radiative forcing and a likely causal relationship with effects on
42 temperature, precipitation, and related climate variables, the non-uniform distribution of ozone
43 (spatially and temporally) makes the development of quantitative relationships between the

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1 magnitude of such effects in differing ozone concentrations in the U.S. challenging. Thus, the
2 Draft Ozone ISA recognizes that “current limitations in climate modeling tools, variation across
3 models, and the need for more comprehensive observational data on these effects represents
4 sources of uncertainty in quantifying the precise magnitude of climate responses to ozone
5 changes, particularly at regional scales. While these complexities affect the EPA’s ability to
6 consider specific ozone concentrations associated with differing magnitudes of climate-related
7 effects, it does give the EPA the ability to estimate growth-related impacts of trees that can
8 inform their consideration of the sequestration of carbon in terrestrial ecosystems, a process that
9 can reduce tropospheric abundance of the pollutant (CO₂) ranked first in importance as a
10 greenhouse gas and radiative forcing agent.

11
12 What Are Important Uncertainties in the Evidence?

13
14 Among the categories of effects identified in past reviews, key uncertainties remain in the current
15 evidence. The category of ozone welfare effects for which current understanding of quantitative
16 relationships is strongest is reduced plant growth. As a result, this category was the focus of the
17 Administrator’s decision making in the last review, with RBL in tree seedlings playing the role of
18 surrogate for the broader array of vegetation related effects that range from the individual plant level
19 to ecosystem services. Limitations in the evidence base and associated uncertainties recognized in
20 the last review remain and include a number of uncertainties that affect characterization of the
21 magnitude of cumulative exposure conditions eliciting growth reductions in U.S. forests.

22
23 As recognized in the last review, there are uncertainties in the extent to which the 11 tree species for
24 which there are established E-R functions encompass the range of ozone sensitive species in the
25 United States and also the extent to which they represent U.S. vegetation as a whole. Therefore, it
26 should not be assumed that species of unknown sensitivity are tolerant to ozone.

27
28 The EPA recognized important uncertainties in extent to which the E-R functions for reduced growth
29 in tree seedlings are also descriptive of such relationships during later life stages for which there is a
30 paucity of established E-R relationships. In addition, the EPA recognizes limitations and their ability
31 to estimate growth effects of tree lifetimes of year to year variation in ozone concentrations. For
32 example, the studies on which the established E-R functions for 11 tree species are based vary in
33 duration (such as 82 days in a single year to 555 days spanning more than one year). In the Draft
34 Ozone PA, the EPA goes to great lengths in walking through uncertainties and recognizing
35 limitations and data interpretation with a number of studies that they have considered. This is not
36 unexpected due to the biological variability in response to a pollutant such as ozone in ecological
37 systems.

38
39 Exposure and Air Quality Information

40
41 In general, the EPA decision making in the last review placed greatest weight on estimates of
42 cumulative exposures to vegetation based on ambient air monitoring data for ozone and
43 consideration of those estimates in light of E-R relationships for ozone related reduction in tree

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1 seedling growth. These analyses supported the consideration of the potential for ozone effects on
2 tree growth and productivity as well as its associated impacts on a range of ecosystem services,
3 including forests, ecosystem productivity, and community composition (80 FR 65292, October 26,
4 2015).

5
6 In revising the standard in 2015 to the current standard, the Administrator concluded that with
7 revision of the standard level, the existing form and averaging time provided the control needed to
8 achieve the cumulative seasonal exposure circumstances identified for the secondary standard. The
9 focus of cumulative seasonal exposure primarily reflects the evidence of E-R relationships for plant
10 growth. The 2015 conclusion was supported by the air quality data analyzed at that time. Analysis in
11 the current review of the still more expanded set of air monitoring data, which includes 1,545
12 monitoring sites with sufficient data for variation of design values, documents similar findings as
13 from the analysis of data from 2000-2013 described in the last review.

14
15 Monitoring sites with lower ozone concentrations as measured by the design value metric (based on
16 the current form and averaging time of the secondary standard) also have lower cumulative seasonal
17 exposures, as quantified by the W126 Index. As the form and averaging time of the secondary
18 standard have not changed since 1997, the analyses performed have been able to assess the control
19 exerted by these aspects of the standard in combinations with reductions in the level (i.e., from 80
20 ppb in 1997 to 75 ppb in 2008 to 70 ppb in 2015) on cumulative seasonal exposures in terms of the
21 W126 Index.

22
23 In Figure 4-7 of the Draft Ozone PA, the evidence currently available leads the EPA to conclusions
24 regarding exposure levels associated with effects as similar conclusions in the last review. Based
25 largely on this evidence in combination with use of RBL as a surrogate, for vegetation related
26 effects, the value of 17 ppm-hrs was the average W126 Index (over three years) was identified in the
27 2015 decision (80 FR 65393; October 26, 2015). As summarized above, the information available in
28 the present review continues to indicate that cumulative seasonal exposure levels at virtually all sites
29 with air quality meeting the current standard fall below the level of 17 ppm-hrs that was identified
30 when the current standard was established (80 FR 65393; October 26, 2015). Additionally, the
31 average W126 Index in Class I areas that meet the current standard for the most recent three-year
32 period is below 17 and at or below 13 ppm-hrs in 44 of those of 46 Class I areas. In addition, in the
33 current Draft Ozone PA, Table 4-2 summarizes distribution of W126 Index values in/near Class I
34 areas. In summary, as is the case at all monitoring sites nationally, sites in or near Class I areas with
35 design values at or below 70 ppb in the most recent three-year period have had a seasonal W126
36 Index (based on three year average) at or below 17 ppm-hrs. As was the case at the time the current
37 standard was established, with the exception of four values that occurred nearly a decade ago in the
38 southwest region, cumulative seasonal exposures in all Class I areas during periods that met the
39 current standard were no higher than 17 ppm-hrs which reflects a protective level in the standard.

40
41 Based on established E-R functions for tree seedling growth reductions in 11 species, the tree
42 seedling RBL for the median tree species is 5.3% for a W126 Index of 17 ppm-hrs, rising to 5.7%
43 for 18 ppm-hrs, 6% for 19 ppm-hrs and 6.4% for 20 ppm-hrs. Below 17 ppm-hrs, median estimates

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1 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.
2 These estimates are unchanged from what was indicated by the evidence in the last review.

3
4 The EPA has focused in the current review on the E-R relationships available in the last review for
5 purposes of considering ozone exposure levels associated with growth-related impacts. Currently
6 available evidence, including the newly available in the Draft Ozone ISA does not indicate the
7 occurrence of ozone-related effects attributable to cumulative ozone exposures lower than was
8 established at the time of the last review (.07 ppm). As in the last review, the currently available
9 evidence continues to support a cumulative, seasonal exposure index as a biologically-relevant and
10 appropriate metric for assessment of the evidence of exposure/risk information for vegetation, most
11 particularly for growth related effects. This is reasonable, responsible, and reflects good use of
12 scientific information by the EPA. The evidence continues to support important roles for cumulative
13 exposure and for weighting higher concentrations over lower concentrations of ozone and ambient
14 air. Thus, among the various such indices considered in the literature the cumulative, concentration-
15 weighted W126 function continues to be best supported for purposes of relating ozone air quality to
16 growth-related effects.

17
18 The RBL appears to be appropriately considered as a surrogate for an array of adverse welfare
19 effects and based on consideration of ecosystem services and potential for impacts to the public as
20 well as conceptual relationships between vegetation growth effects and ecosystem scale effects.
21 Biomass loss is a scientifically sound surrogate of a variety of adverse effects that could be exerted
22 to public welfare. In the previous review, the Administrator used RBL as a surrogate for
23 consideration of the broader array of vegetation related effects of potential welfare significance that
24 included effects of growth of individual sensitive species and extended to ecosystem level effects
25 such as community composition in natural forests, particularly in protected public lands (80 FR
26 65406, October 26, 2015). The EPA believes, and the CASAC concurs, that information available in
27 the present review does not call into question this approach, indicating there continues to be support
28 for the use of tree seedling RBL as a proxy for the broader array of vegetation-related effects, most
29 particularly those related to growth.

30
31 To What Extent Does the Available Information Alter Our Understanding of the Magnitude of
32 Growth Reductions Expected to be of Public Welfare Significance?

33
34 It was recommended in the last review that a 6% RBL was “unacceptably high” and endeavored to
35 identify a secondary standard that would limit three-year average ozone exposures somewhat below
36 W126 Index values associated with a 6% RBL in the median species. This led to identification of a
37 seasonal W126 Index value of 17 ppm-hrs that the Administrator concluded was appropriate as a
38 target at or below which the new standard would generally restrict cumulative seasonal exposures
39 (80 FR 65407, October 26, 2015). The currently available evidence continues to indicate conceptual
40 relationships between reduced growth and the broader array of vegetation-related effects of ambient
41 ozone exposure.

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1 What Does the Information Available in the Current Review Indicate with Regards to Support for
2 Use of a Three Year Average Seasonal W126 Index as the Cumulative Exposure Metric (Associated
3 with a Value of 17 ppm-hrs) for Describing the Requisite Level of Protection for the Secondary
4 Standard?
5

6 In the setting of the current standard, the EPA focused on control of seasonal cumulative exposures
7 in terms of a three year average W126 Index metric. The evaluations in the PA for the last review
8 recognized there to be limited information to discern differences in the level of protection afforded
9 for cumulative growth-related effects by a standard focused on a single-year W126 as compared to a
10 three-year W126 Index (80 FR 65390, October 26, 2015). Accordingly, the identification of the three
11 year average for considering the seasonal W126 Index recognized that there was year-to-year
12 variability, not just in ozone concentrations, but also in environmental factors, including rainfall and
13 meteorological factors, that influences the occurrence and magnitude of ozone related effects in any
14 year and contribute uncertainties to interpretation of the potential for harm to public welfare over the
15 longer term. Based on this recognition, as well as other considerations, the Administrator expressed
16 greater confidence in judgements related to public welfare impacts based on seasonal W126 Index
17 estimated by a three-year average and accordingly relied on that metric, which appears of reasonable
18 thought and scientifically sound.
19

20 Does the Currently Available Scientific Evidence in Air Quality and Exposure Analyses Support or
21 Call into Question the Adequacy of the Protection Afforded by the Current Secondary Ozone
22 Standard?
23

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

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

3
4 As was the case in the last review, a category of effects for which the evidence supports quantitative
5 description of relationships between air quality conditions and response is plant growth or yield. The
6 evidence base continues to indicate growth-related effects as sensitive welfare effects, with the
7 potential for ecosystem scale ramifications. For this category of effects, there are established E-R
8 functions that relate cumulative seasonal exposure of varying magnitudes to various incremental
9 reductions in expected tree seedling growth (in terms of RBL) and in expected crop yield. Decades
10 of research also recognizes visible foliar injury as an effect of ozone, although uncertainties continue
11 to hamper efforts to quantitatively characterize the relationship of its occurrence and relative severity
12 with ozone exposures.

13
14 Reviews of NAAQS also required judgements on the extent to which particular welfare effects (such
15 as with regard to type, magnitude/severity, or extent) are important from a public welfare
16 perspective. In the case of ozone, such a judgement includes consideration of the public welfare
17 significance of small estimates of RBL and associated unquantified potential for larger scale effects.
18 With regard to public welfare significance of 5-6% RBL, the EPA notes CASAC characterization of
19 6% RBL (in seedlings of median tree species) in the last review. The rationale provided by the
20 CASAC with this characterization was primarily conceptual and qualitative rather than quantitative.
21 The conceptual characterization recognized linkages between effects on the plant level scale and
22 broader ecosystem impacts, and this facilitated the Administrator consider RBL as a surrogate for
23 the broader impacts that could be elicited by ozone. In the 2015 decision, the Administrator took
24 note of CASAC advice regarding use of RBL as a proxy and set the standard with “underlying
25 objective of a revised Secondary Standard that would limit cumulative exposures in nearly all
26 instances to those for which the median RBL estimate would be somewhat lower than 6%” (80 FR
27 65407, October 26, 2015). The 2015 decision noted that “the Administrator does not judge RBL
28 estimates associated with marginal higher exposures [at or above 19 ppm-hrs] in isolated rare
29 instances to be indicative of adverse effects to the public welfare” (80 FR 65407, October 26, 2015).

30
31 In considering the quantitative analyses available in the Draft Ozone PA, the EPA noted the findings
32 from the analysis of recent air quality at sites across the United States, including in or near 64 Class I
33 areas and also analysis of historical air quality. Findings from the analysis of air quality data from
34 the most recent period and from the larger analysis of historical air quality data extended back to
35 2000 are consistent with the air quality analysis findings that were part of the basis for the current
36 Standard. That is, in virtually all design value periods and in all locations at which the current
37 Standard was met, the three-year average W126 metric was at or below 17 ppm-hrs, the target
38 identified by the Administrator in establishing the current standard (80 FR 65404-65410, October
39 26, 2015).

40
41 The EPA summarized in the Draft Ozone PA that there is little in the information available in the
42 current review that differs from that in the last review that relate to key aspects of the judgments and
43 associated decision that established the current standard in 2015. The new information available is

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1 consistent with that available in the last review for the principle effects for which the evidence is
2 strongest (such as growth, reproduction, and related larger scale effects, as well as visible foliar
3 injury).

4
5 General Comments
6

- 7 1. The CASAC compliments the EPA on a very thorough and well-written Chapter 4.
- 8 2. The foundation upon which scientific data was utilized while also incorporating concepts of
9 judgement on behalf of the EPA with input from various entities lays a strong and clear scientific
10 process of considerations for the preliminary conclusions on the current secondary standard.
- 11 3. The preliminary conclusion by the EPA that the 2015 decision to revise the level of the
12 secondary standard for photochemical oxidants, including ozone to .07 ppm (70 ppb) in
13 conjunction with retaining the indicator (O₃), averaging time (8 hours) and form (4th highest
14 annual daily maximum 8-hour average concentration, averaged across three years) appears to be
15 working in maintaining ambient air concentrations of ozone across the United States at levels
16 that are protective for the public welfare, particularly as related to vegetation.
- 17 4. RBL appears to be appropriately considered as a surrogate for an array of adverse welfare effects
18 and based on consideration of ecosystem services and potential for impact to the public as well
19 as conceptual relationships between vegetation growth effects and ecosystem scale effects. The
20 CASAC agrees that biomass loss, as reported in RBL, is a scientifically-sound surrogate of a
21 variety of adverse effects that could be exerted to public welfare.
- 22 5. The EPA believes, and the CASAC concurs, that information available in the present review
23 does not call in to question this RBL approach, indicating there continues to be support for the
24 use of tree seedling RBL as a proxy for the broader array of vegetation related effects, most
25 particularly those related to growth that could be impacted by ozone.
- 26 6. It was recommended in the last review that a 6% RBL was “unacceptably high” and endeavored
27 to identify a secondary standard that would limit three-year average ozone exposure somewhat
28 below W126 Index values associated with a 6% RBL in the median species, and the CASAC
29 concurs that this strategy is still scientifically reasonable. The identification of a seasonal W126
30 Index value of 17 ppm-hrs that the EPA concludes appropriate as a target at or below which the
31 Secondary Standard would generally restrict cumulative seasonal exposure. The CASAC
32 believes that this target is still effective in particularly protecting the public welfare in light of
33 vegetation impacts from ozone.
- 34 7. On August 23, 2019, the D.C. Circuit Court issued an opinion concluding, in relevant part, that
35 the EPA had not provided a sufficient rationale for aspects of its decision on the 2015 secondary
36 standard (Murray Energy v. EPA, 936 F.3d 597 [D.C. Cir. 2019]). Accordingly, the court
37 remanded the secondary standard to the EPA for further justification or reconsideration,
38 particularly in relation to its decision to focus on a 3-year average for consideration of the
39 cumulative exposure, in terms of W126, identified as providing requisite public welfare
40 protection, and its decision to not identify a specific level of air quality related to visible foliar
41 injury. It is not clear if the EPA has fully addressed this concern in the Draft Ozone PA.

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- 1 8. Figure 4D-3 containing a scatter plot of W126 versus 8-hour ozone design values based on 2015-
2 2017 data should be included in Chapter 4 to justify the use of the 8-hour ozone design as a
3 surrogate for W126.
- 4 9. The CASAC recommends that the Draft Ozone PA should more thoroughly address effects of
5 ozone on climate change by providing quantitative estimates and uncertainty bands for effects of
6 ozone on global warming and the consequence for economic and welfare effects on the United
7 States. At a minimum, estimates of the change in warming caused by a change in ozone should
8 be discussed and implications for human welfare in the United States should be evaluated.
- 9 10. The approach described in Chapter 4 to considering the evidence for welfare effects is laid out
10 very clearly, thoroughly discussed and documented, and provided a solid scientific underpinning
11 for the EPA conclusion leaving the current secondary standard in place.
12
13
14
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16

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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)

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4
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7
8
9 **Dr. James Boylan** A-2
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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?

O₃ and Photochemical Oxidants in the Atmosphere (Section 2.1)

This section should discuss how the precursor emissions listed in this section (NO_x, VOCs, CO, and CH₄) 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 NO_x 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 O₃ 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, NO_x emissions from electric generating

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1 units (EGUs) have low uncertainty since they are typically captured by hourly CEMs. On the other hand,
2 other source sectors and pollutants may be highly uncertain. The uncertainties in the emissions inventory
3 (magnitude, spatial allocation, and temporal allocation) should be discussed for each pollutant and
4 source sector. In addition, it would be helpful to add national maps containing county-level emissions
5 for NO_x, VOCs, CO, and CH₄ to show the variability across the country.
6

7 It is not clear if CH₄ is included in the VOC emissions or not. The text should clearly state if CH₄ is
8 included or excluded from the VOC emissions discussed in this Chapter.
9

10 Ozone in Ambient Air (Section 2.4)

11 This section should include a discussion on ozone precursor trends in addition to ozone trends.
12 Specifically, trends in NO_x, VOCs, and CO measurements from national monitoring networks (AQS,
13 near-road, NCore, and PAMS) should be included and discussed.
14

15 It is stated on page 2-19, “B shows the seasonal pattern for an urban site in Baton Rouge, LA.
16 Throughout the southeastern U.S., the highest O₃ concentrations are often observed in April and May
17 due to the onset of warm temperatures combined with abundant emissions of biogenic VOCs at the start
18 of the growing season. This is often followed by lower concentrations during the summer months, which
19 is associated with high humidity levels that tend to suppress O₃ formation.” While this statement might
20 be true for Baton Rouge, it does not apply to the entire southeastern U.S. In addition, a reference should
21 be provided to support the statement that high humidity levels suppress O₃ formation.
22

23 EPA’s 2016 Exceptional Events Rule allows certain ozone measurements due to natural events to be
24 excluded from the official design values when compared to the NAAQS. In some cases, identical
25 exceptional events can be treated differently in one location vs. another based on how close the area is to
26 the standard. In both locations, people are impacted by adverse health effects, but the data is removed in
27 one location and not the other. The PA should discuss how exceptional events are accounted for in the
28 policy assessment.
29

30 Background O₃ (Section 2.5)

31 EPA used the CMAQ chemical transport model with the zero-out approach to estimate U.S. background,
32 international, and natural contributions. Figures 2-22, 2-23, and 2-24 should add a 100% line. EPA
33 should add explanations for values over the 100% line. The caption in Figure 2-26 is incorrect. The
34 figures and tables containing USB contribution on the average of the top 10 predicted O₃ days and the
35 4th highest O₃ days are very useful and relevant to policy decisions. These values should be compared to
36 previous work by Jaffe (2018) and Parrish (2017, 2019). In Appendix 2B, the scale used in Figure 2B-15
37 should be reduced from 100% to a lower value to allow the reader to see the differences between
38 monitoring sites.
39
40

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1 **Chapter 3 – Review of the Primary Standard**
2

3 *What are the CASAC views on the approach described in chapter 3 to considering the health effects*
4 *evidence and the risk assessment in order to inform preliminary conclusions on the primary standard?*
5 *What are the CASAC views regarding the key considerations for the preliminary conclusions on the*
6 *current primary standard?*
7

8 The more detailed discussion on selection of study areas should be moved from Section 3D.2.1 to
9 Section 3C.2 since Appendix 3C is presented prior Appendix 3D. Sacramento (2017 design value = 86
10 ppb) does not meet the second selection criteria listed on page 3D-14, “Combined statistical area
11 (CSA)/metropolitan statistical area (MSA) ambient air 24 monitor design values are between 60-80 ppb,
12 thus having minimal adjustment needed to just meet the current 8-hr O₃ NAAQS”. A reason for
13 selecting this study area should be added to the document.
14

15 The CAMx chemical transport model was only run with 2016 meteorology while the APEX exposure
16 model was run using 2015-2017 meteorological data. This Chapter should give a high-level explanation
17 of how these two models were combined to generate 2015-2017 exposures with a reference to the
18 Appendix for additional details.
19

20 A comparison of 2016 emissions used in the CAMx model (Table 3C-4) to the 2014 NEI emissions
21 (Figure 2-1) show similar emissions for CO and VOCs (after adjusting for year specific biogenic
22 emissions). However, the anthropogenic NO_x emissions in 2016 are 20% lower than the anthropogenic
23 NO_x emissions in 2014. This large difference should be explained.
24

25 EPA performed an ozone model performance evaluation (MPE) for each study area. However,
26 additional explanation is needed to describe the time series plots shown in pages 3C-34 – 3C-61. It
27 appears that the measured maximum daily 8-hour average ozone (MDA8) is averaged for all monitors in
28 an area and compared to the modeled MDA8 average for all monitors in the study area. The document
29 should explain how the modeled MDA8 average is calculated when observations are missing. For
30 example, do the corresponding model results get removed or do they remain in the average? Also, it
31 appears that the “# of sites” included in the top right corner of each plot includes both CSA and “buffer”
32 sites. It would be more informative to evaluate sites inside the CSA and outside the CSA (the “buffer”
33 sites) separately. In fact, it would be most informative to develop individual time series plots for each
34 monitoring site included in each study area. The “# of sites” shown in Figure 3C-25 for Atlanta in
35 January is “14”. However, Georgia only has two year-round monitors in the state. For each study area
36 and season, it would be useful to plot all hourly observed and modeled concentrations in a single 24-
37 hour diurnal plot with means and standard deviations (similar plot as Figure 3C-67).
38

39 The document should include the number of monitors used in each model performance summary table
40 contained on pages 3C-31 – 3C-59. It is unclear if the “buffer” sites are included along with the CSA

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1 sites. Again, it would be more informative to evaluate sites inside the CSA and outside the CSA (the
2 “buffer” sites) separately for each study area.

3
4 In addition to the ozone MPE, it would useful to perform a model performance evaluation for the ozone
5 precursors (NO_x and VOCs). If the precursor concentrations don’t match the observations, the HDDM
6 sensitivity results may not be accurate even if the ozone concentrations match observations.

7
8 Figures 3C-67 and 3C-75 for Atlanta are both missing the “75 ppb” ozone distributions. Although NO_x
9 emissions were not adjusted in Atlanta for the 75 ppb scenario, the modeling results for the 75 ppb
10 scenario should still be included.

11
12 Section 3C.5.2.2.3 should discuss why NO_x reductions alone were selected for adjusting design values.
13 In many cases, VOC reductions occur simultaneously with NO_x reductions. Also, many areas of the
14 county are equally as sensitive to VOC reductions as NO_x reductions.

15
16 Table 3C-19 containing percent emissions changes used for each urban area to just meet each of the 22
17 air quality scenarios evaluated should include a negative (-) sign for emission reductions.

18
19 It is stated on page 3-35 that “In 2016, nearly 50% of jobs held by civilian workers required outdoor
20 work at some point during the workday.” On page 3-56, it is stated “The exception to this is for outdoor
21 workers, who due to the requirements of their job spend more time outdoors. As information for this
22 group, including specific durations of time spent outdoors and activity data, is limited, the group was not
23 simulated in this assessment, although we note that a targeted analysis was performed in the 2014
24 HREA.” The footnote on page 3-57 states “Outdoor workers are not a population that has been explicitly
25 simulated in the current analyses, and the updates to exposure duration and target ventilation rate in the
26 current simulations would be expected to produce different results than those estimated for the 2014
27 REA.” The PA should explain why outdoor workers were not simulated in the current analyses and if
28 this would have a significant impact on the risk assessment.

29
30 Section 3C.6 discusses interpolation of adjusted air quality using Voronoi Neighbor Averaging (VNA).
31 A justification for choosing VNA over other methods should be included and its uncertainty quantified.

32
33 The exposure and risk results from the 7 study areas that are in common with the 2014 ozone HREA
34 review should be compared and similarities/differences discussed in this document.

35
36 The current form of the standard is discussed in Section 3.1.2.3. For the previous three ozone standards,
37 the form has been the annual fourth-highest daily maximum 8-hour ozone average concentration,
38 averaged over 3 years. The PA discusses the findings that this form better represents the continuum of
39 health effects associated with increasing ozone concentrations compared to the exceedance form of the
40 previous 1-hour ozone standard. Consideration was given to the fifth-highest value and the use of a

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1 percentile-based form. In addition, it was recognized that this form of the standard provides stability
2 with regard to implementation of the standard. However, the PA does not discuss the possible use of an
3 “integrated” form of the standard (e.g., average of 10 highest daily maximum 8-hour ozone average
4 concentrations).

5
6 Conceptually, an “integrated” form of the standard should provide a better representation of the
7 continuum of health effects associated with increasing ozone concentrations. Typically, the higher end
8 of the daily maximum 8-hour ozone average concentration distribution drives health effects. The current
9 form of the standard throws away the three highest concentrations (which typically would have the most
10 significant health impacts) and ignores other potentially high concentrations beyond the fourth-highest
11 daily maximum 8-hour ozone average concentration. This means that the entire ozone season is
12 characterized by a single 8-hour average ozone measurement. As a result, a monitor that measures three
13 high ozone values (e.g., 100, 98, 95 ppb) and the fourth-high value is 70 ppb, would have the same
14 fourth-high value as another monitor which measures 70 ppb for each of its four highest concentrations.
15 In addition, the remainder of the higher end of the daily maximum 8-hour ozone average concentration
16 distribution is ignored (i.e., fifth-high, sixth-high, seventh-high, eighth-high, ninth-high, and tenth-high).
17 An integrated form of the standard (e.g., 10-day average vs. fourth-highest value) would be able to better
18 account for these higher concentrations as part of a multi-day average of daily maximum 8-hour ozone
19 average concentrations. In addition, an integrated form of the standard would provide greater stability
20 than the current form of the standard with regard to implementation of the standard.

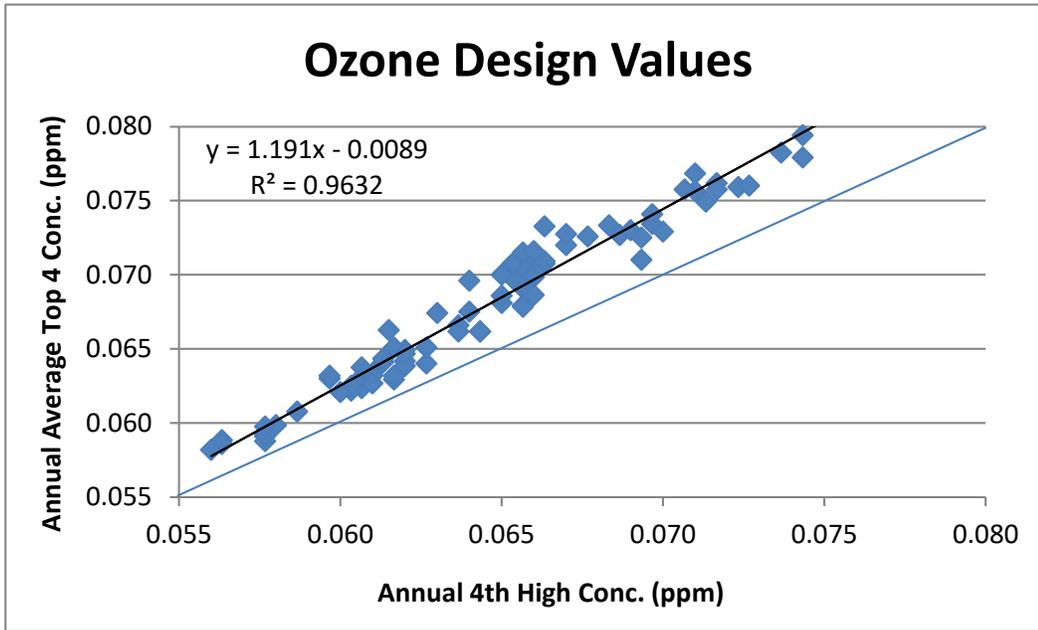
21
22 EPA should compare the current form of the standard against various integrated forms of the standard to
23 determine if the relationship is linear (r^2 near 1.00) and if the current form of the standard is appropriate
24 for representing the continuum of health effects associated with increasing ozone concentrations.

25
26 Georgia EPD examined the current form of the standard against various integrated forms of the standard
27 (average of the top 4 and average of the top 10 daily maximum 8-hour ozone average concentrations) at
28 all 23 ozone monitors in the state of Georgia for 2013-2018. Comparisons were made for annual values
29 (2013-2018) and 3-year design values (2015-2018). The ozone design value r^2 for the current form of
30 the standard vs. the average of the top 4 daily maximum 8-hour ozone average concentrations was 0.963
31 (Figure 1). The ozone design value r^2 for the current form of the standard vs. the average of the top 10
32 daily maximum 8-hour ozone average concentrations was 0.979 (Figure 2). This indicates that the
33 current form of the standard is appropriate to represent the upper part of the ozone concentration
34 distribution in Georgia. A similar type of analysis should be performed for the entire country (either
35 state-by-state or region-by-region) to determine if the current form of the ozone standard is appropriate
36 nation-wide.

37

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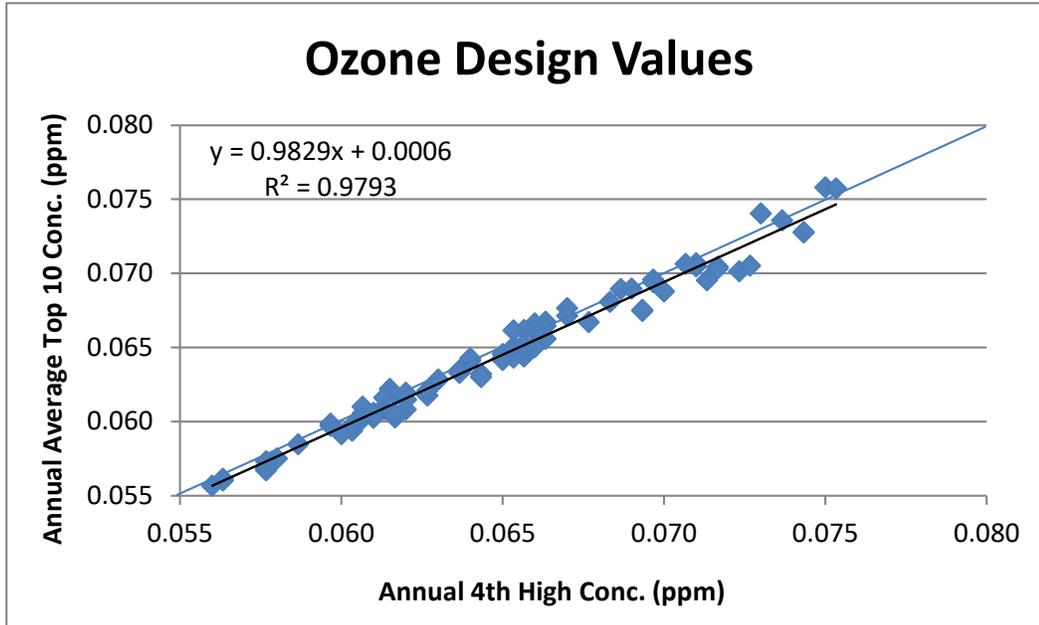


1
2 **Figure 1.** Comparison of the 3-year ozone design values (2015-2018) using the annual 4th high daily
3 maximum 8-hour ozone average concentration vs. the annual average of the top 4 daily maximum 8-
4 hour ozone average concentrations.
5

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1



2

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

6

7

8 **Chapter 4 – Review of the Secondary Standard**

9

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

14

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

23

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

4
5 **Chapters 3 and 4**

6
7 *What are the CASAC views regarding the areas for additional research identified in Chapters 3 and 4?*
8 *Are there additional areas that should be highlighted?*
9

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

15
16 **References**

- 17
18 Jaffe D. A., et al. (2018) Scientific assessment of background ozone over the U.S.: Implications for air
19 quality management. Elem. Sci. Anth., 6 56 doi.org/10.1525/elementa.309.
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21 Parrish, D. D., Young, L. M., Newman, M. H., Aikin, K. C., and Ryerson, T. B. (2017) Ozone Design
22 Values in Southern California's Air Basins: Temporal Evolution and U.S. Background Contribution, J.
23 Geophys. Res.-Atmos., 122, 11166–11182, <https://doi.org/10.1002/2016JD026329>.
24
25 Parrish, D. D. and C. A. Ennis (2019). Estimating background contributions and US anthropogenic
26 enhancements to maximum ozone concentrations in the northern US, Atmos. Chem. Phys., 19, 12587–
27 12605, <https://doi.org/10.5194/acp-19-12587-2019>.
28
29

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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:

- (3) 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.
- (4) 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

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- 1 b. Better characterize dose-dependent thresholds and causal biological C-R functions for
2 pulmonary inflammation and other physiological responses in other tissues, organs, and
3 systems in response to inhaled ozone.
4

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

- 9 7. *Summarize available empirical evidence on how changes in public health effects depend on*
10 *changes in ozone levels.* Ideally, this information should be discussed in detail in the final ISA.
11 8. *Summarize results from a systematic review and critical evaluation and synthesis of relevant*
12 *studies relied on to reach conclusions,* including negative studies and studies of nonlinear C-R
13 functions for ozone that were omitted in the draft ISA but that should inform the PA.
14 9. Throughout the PA, *clearly distinguish between causal C-R functions (describing how public*
15 *health risks change in response to changes in ambient ozone levels) and regression C-R*
16 *functions (describing how observed public health risks differ across different observed or*
17 *estimated ambient ozone levels).* These are in general different concepts and different curves.
18 Causal C-R functions are relevant for policy analysis. The draft PA addresses regression C-R
19 functions. The final PA should use validated causal C-R functions to predict effects of alternative
20 policy choices.
21 10. *Increase transparency and logical soundness in deriving conclusions* by documenting exactly
22 how conclusions were reached and validated, in enough detail so that others can trace and check
23 the logic used. This documentation should provide clear operational definitions of the key
24 quantities and terms used to calculate, validate, and communicate scientific results. Conclusions
25 should address the extent to which changing NAAQS standards for ozone demonstrably causes
26 changes in public health outcomes. Uncertainties and variability in the answers should be
27 quantified.
28 11. *Distinguish between estimated and actual exposures* throughout the PA.
29 12. *Discuss in more detail causal biological mechanisms of inflammation-related health effects*
30 *preventable by reducing current ozone levels (including, if relevant, roles of the NLRP3*
31 *inflammasome in mediating persistent adverse health effects).*
32 13. *Critically discuss the biological realism* of the PA’s risk predictions and modeling assumptions,
33 specifically for how public health risks are predicted to change in response to changes in ambient
34 ozone levels.

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- 1 14. *Present results of empirical validation tests* of the PA’s risk predictions and modeling
2 assumptions against observations, specifically for how public health risks have changed in
3 response to changes in ambient ozone levels.
- 4 15. *Quantify uncertainty and variability in risk predictions, taking into account epistemic*
5 *uncertainties (e.g., from model uncertainty and exposure estimation error) as well as sampling*
6 *variability. Present comprehensive, quantitative uncertainty, sensitivity, and variability analyses*
7 showing how the ISA’s conclusions change for variations in selection and weighting of studies,
8 compositions of populations (representing causally relevant interindividual variability and
9 heterogeneity in causal C-R functions), modeling choices and assumptions, interpretations of
10 undefined and vague terms, and subjective judgments on which the conclusions depend. These
11 comprehensive analyses should complement the limited set of uncertainty and variability
12 analyses in Section 3D of the draft PA.

13
14
15 **Chapter 3 – Review of the Primary Standard**

16
17 *What are the CASAC views on the approach described in chapter 3 to considering the health effects*
18 *evidence and the risk assessment in order to inform preliminary conclusions on the primary standard?*
19 *What are the CASAC views regarding the key considerations for the preliminary conclusions on the*
20 *current primary standard?*

21
22 Chapter 3 and its supporting appendixes predict risks using models and assumptions that have not been
23 validated for predicting how changes in ozone affect public health risks. It omits important caveats such
24 as those provided in the 2014 REA
25 (www3.epa.gov/ttn/naaqs/standards/ozone/data/20140829healthrea.pdf). These included the following
26 for the 2012 MSS model (emphases added):

- 27 • “Clearly the **intra-individual variability**... in the MSS model is a key parameter and is
28 influential in predicting the proportions of the population with FEV1 decrements > 10 and 15%.
29 **The assumption that the distribution of this term is Gaussian is convenient for fitting the**
30 **model, but is not accurate.** The extent to which this mis-specification affects the estimates of
31 the parameters of the MSS model and its predictions is not clear.”
- 32 • “Although **the model does not have good predictive ability** for individuals (psuedo-R2 0.28), it
33 does better at predicting the proportion of individuals with FEV1 decrements. 10, 15, and 20%
34 (psuedo-R2s of 0.78, 0.74, 0.68) (McDonnell et al., 2012). The clinical studies that these model
35 estimates are based on were conducted with young adult volunteers rather than randomly
36 selected individuals, so **it may be that selection bias has influenced the model parameter**
37 **estimates.** The parameter estimates are not very precise, partly as the result of correlations
38 between the parameter estimates... The MSS model is also sensitive to the exposure

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1 concentrations, but we have not quantified that sensitivity. ... **We are unable to properly**
2 **estimate the true sensitivities or quantitatively assess the uncertainty of the MSS model.** ...
3 As discussed in Section 6.5.3 below, there are uncertainties in extrapolating the MSS model
4 down to age 5 from the age range of 18 to 35 to which the model was fit. ...[T]he uncertainty of
5 the extension to children of the MSS model could be substantial.” Section 6.5.7 adds that “EPA
6 staff have identified key sources of uncertainty with respect to the lung function risk estimates.
7 These are: the physiological model in APEX for ventilation rates, the O₃ exposures estimated by
8 APEX, the MSS model applied to ages 18 to 35, and extrapolation of the MSS model to children
9 ages 5 to 18. ... At this time **we do not have quantitative estimates of uncertainty for any of**
10 **these.”**

11
12 The Draft PA does state that “We are using this model to estimate lung function decrements for people
13 ages 5 and older. However, this model was developed using only data from individuals aged 18 to 35
14 and the age adjustment term [$\beta_1 + \beta_2 (\text{Age}_{ijk} - 23.8)$] in the numerator of Equation 3D-13 is not
15 appropriate for all ages.” However, the fact that the model predictions are based on assumptions that are
16 unlikely to be accurate (e.g., that the parameter alpha 2 in Table 3D-21 quadruples on one’s 18th
17 birthday) and that the models and their predictions have not been empirically validated or verified
18 should be emphasized. In effect, the PA selects some specific parametric models and uses them to make
19 risk predictions, but the validity of the models and their predictions is unknown.

20
21 The final PA should discuss empirical validation of model predictions for changes in public health risks
22 caused by changes in ambient ozone levels across a variety of settings. It should explicitly address the
23 extent to which the property of invariant causal prediction has been validated for the models used to
24 make predictions of the effects of potential future changes in policies. It should comment on the internal
25 and external validity of the risk models and their predictions, and should present the results of empirical
26 validation tests for the risk models and predictions. Chapter 3 and its appendices should clearly
27 distinguish between *causal* C-R functions (describing how public health risks change in response to
28 changes in ambient ozone levels) and *regression* C-R functions (describing how observed public health
29 risks differ across different observed or estimated ambient ozone levels). These are in general different
30 concepts and different curves. Causal C-R functions are relevant for policy analysis. The draft PA
31 addresses regression C-R functions. The final PA should use validated causal C-R functions (satisfying
32 the property of invariant causal prediction if possible) to predict effects of alternative policy choices.

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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.

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

3
4 4. The current ozone NAAQS level of 70 ppb does not provide an adequate margin of safety for children
5 with asthma.

6
7 **1. Asthma** is a complex disease [1]. It involves airflow limitation, airway inflammation, and nonspecific
8 airways hyperresponsiveness. Injury to, and increased permeability of, the airway epithelium is an
9 increasingly recognized feature of the disease. Remodeling of the airways is also part of asthma, with
10 thickening of the submucosal basement membrane consistently seen in lung biopsies of people with
11 asthma, even in those with normal pulmonary function.

12
13 Many people with asthma have normal lung function and are asymptomatic at baseline, but other
14 features of the disease, including airway inflammation and airways hyperresponsiveness, persist even
15 when they are in remission from the symptoms of the disease. Most children with asthma are able to be
16 active and exercise outdoors. They develop problems when something triggers an exacerbation, such as
17 exposure to an allergen to which they are sensitized, a respiratory infection, or air pollutants, among
18 others. Arguably the most important potential adverse effect of acute ozone exposure in a child with
19 asthma is not whether it causes a transient decrement in lung function, but whether it causes an asthma
20 exacerbation.

21
22 **2. Ozone has respiratory effects** beyond its well-described effects on lung function. It increases airway
23 inflammation, a key component in the pathophysiology of asthma. Eosinophilic inflammation is
24 particularly important in allergic asthmatics, and we know from clinical studies that airway eosinophilia
25 is increased in response to ozone exposure in asthmatics. Ozone increases non-specific airways
26 hyperresponsiveness in clinical studies. And ozone exposure causes airway epithelial injury and
27 increases airway epithelial permeability, both cardinal features in asthma pathophysiology. This
28 increases the potential for materials deposited in the distal airways, such as particles or allergens, to
29 access the lung interstitium and vascular space. These effects beyond lung function decrements likely
30 contribute to the risk of an asthma exacerbation. Yet they are not captured or considered in the risk
31 analysis.

32
33 EPAs current approach minimizes/ignores the full spectrum of potential ozone airway effects. The
34 human clinical studies indicate that both lung function decrements and increased airway inflammation
35 result from exposures as low as 60 ppb in the 6.6-hr studies. The focus in the risk assessment is solely on
36 FEV₁, because that database is robust. But we know from other studies that the FEV₁ response and the
37 airway inflammatory response occur via different mechanisms [2-4], and some people are more prone to
38 one of these effects than the other. This means that there are individuals who will experience increases
39 in airway inflammation without lung function decrements or symptoms. The absence of symptoms could

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1 result in a failure of the individual to limit exposure, thereby further worsening the airway inflammatory
2 effect of the exposure.

3
4 It is reasonable to expect that, in people with asthma, an increase in airway inflammation is an adverse
5 effect, with the potential to increase the risk for an asthma exacerbation. Repeated episodes of airway
6 inflammation may enhance airway remodeling, which occurs in asthma, and leads to irreversible
7 reductions in lung function.

8
9 Studies in smokers provide additional evidence that adverse respiratory effects of ozone can occur in the
10 absence of lung function decrements. Current active smokers are generally unresponsive to the lung
11 function decrements of ozone exposure [5], but still may experience airway inflammation [2], and may
12 be at risk for increased oxidative stress effects, because their alveolar macrophages are primed by the
13 smoking [6].

14
15 **3. The ozone PA makes the following assumptions:**

16
17 **a. Lung function decrements in response to 7-8 hour exposures near 70 ppb are the same in asthmatic**
18 **children as they are in healthy adults.**

19
20 The clinical data in people with mild to moderate asthma, exposed at higher concentrations than those
21 directly relevant to the standard, suggest that asthmatics do not have markedly increased FEV₁ declines
22 compared with healthy subjects. But it is inappropriate to assume that this extends to lower
23 concentrations, or to people with more severe disease. Asthmatics do appear to experience greater
24 effects on measures of airway obstruction, including airways resistance testing. This is briefly reviewed
25 in the ISA, but not considered in the risk assessment. None of the low-concentration, 6 to 7 hr studies
26 listed in Tables 3A-1 and -2 included asthmatics. And very few clinical studies have included severe or
27 even moderate asthma, let alone asthmatic children. And none have included unstable asthmatics or
28 those prone to exacerbations. This is a key knowledge gap, and raises legitimate questions about
29 whether the current standard provides an adequate margin of safety for people with asthma.

30
31 **b. Absence of symptoms means less adversity.**

32
33 The PA seems to suggest that lung function decrements in the absence of symptoms do not represent an
34 adverse health effect. But this should not apply to children with asthma.

35
36 **c. Lung function and other respiratory effects are rapidly reversible in asthmatic children, similar to**
37 **healthy adults.**

38

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1 The time course of the pulmonary function response is well established in healthy adults, but less well in
2 children, and especially in children with asthma. We have no data on the persistence of respiratory
3 effects in asthmatics following low-concentration, more prolonged exposures.
4

5 **4. The current ozone NAAQS level of 70 ppb does not provide an adequate margin of safety for**
6 **children with asthma.**
7

8 The EPA focuses almost exclusively on lung function effects in its risk assessment because of the
9 abundant human data on that measurement. The databases for ozone effects on airway inflammation,
10 nonspecific airway hyperresponsiveness, airway epithelial injury, and epithelial permeability are much
11 more limited than for lung function responses, in part because of greater challenges in measurement.
12 However, the current analysis ignores the possibility, and in fact the likelihood, that transient lung
13 function decrements may not be the most adverse effect of ozone exposure, especially for people with
14 abnormal airways at baseline, as in asthma or COPD. We know from the clinical studies, cited in the
15 ISA and the PA, that 0.60 ppb ozone exposure for 6.6 hrs with exercise increases airway inflammation
16 (in addition to causing lung function decrements) in healthy people. Airway inflammation and other
17 effects need to be considered in the risk assessment because of their relevance in chronic lung disease,
18 especially asthma. The exposure analysis tells us that up to 11% of asthmatic children will experience
19 exposures of this magnitude in areas that just meet the current standard of 70 ppb. We don't know with
20 any certainty how many of those children would/will experience worsening of their asthma as a
21 consequence. But the clinical rationale supporting such a risk is compelling. The epidemiological
22 studies, despite their remaining uncertainties, support this concern. It therefore seems clear that a
23 NAAQS level of 0.70 ppb does not provide an adequate margin of safety, especially for people with
24 airways disease such as asthma.
25

26 CASAC recognized this in its advice to the EPA during the 2014 review:
27

28 "The CASAC advises that, based on the scientific evidence, a level of 70 ppb provides little margin of
29 safety for the protection of public health, particularly for sensitive subpopulations. In this regard, our
30 advice differs from that offered by EPA staff in the Second Draft PA. At 70 ppb, there is substantial
31 scientific evidence of adverse effects as detailed in the charge question responses, including decrease in
32 lung function, increase in respiratory symptoms, and increase in airway inflammation. Although a level
33 of 70 ppb is more protective of public health than the current standard, it may not meet the statutory
34 requirement to protect public health with an adequate margin of safety. In this regard, the CASAC
35 deliberated at length regarding advice on other levels that might be considered to be protective of public
36 health with an adequate margin of safety. For example, the recommended lower bound of 60 ppb would
37 certainly offer more public health protection than levels of 70 ppb or 65 ppb and would provide an
38 adequate margin of safety. Thus, our policy advice is to set the level of the standard lower than 70 ppb
39 within a range down to 60 ppb, taking into account your judgment regarding the desired margin of safety

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1 to protect public health, and taking into account that lower levels will provide incrementally greater
2 margins of safety.

3 [Letter from H. Christopher Frey, CASAC Chair, to Gina McCarthy, EPA Administrator, dated June 26,
4 2014, p. ii,

5 [https://yosemite.epa.gov/sab/sabproduct.nsf/5EFA320CCAD326E885257D030071531C/%24File/EPA-](https://yosemite.epa.gov/sab/sabproduct.nsf/5EFA320CCAD326E885257D030071531C/%24File/EPA-CASAC-14-004+unsigned.pdf)
6 [CASAC-14-004+unsigned.pdf.](https://yosemite.epa.gov/sab/sabproduct.nsf/5EFA320CCAD326E885257D030071531C/%24File/EPA-CASAC-14-004+unsigned.pdf)]

7 Based on what we know about ozone respiratory effects presented in the ISA, and what we know about
8 the nature of asthma, CASAC’s advice in 2014 appears to be relevant for the current review.

9

10 **Additional Comments**

11

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

14

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

20

21 P. 3D-80. For the MSS model, lung function decrements are assumed to be 0 for age >55 yrs. This
22 model does not incorporate newer data on lung function effects in healthy older subjects [7], which
23 demonstrated lung function effects in subjects older than 55 yrs. This should be acknowledged in the
24 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 (O₃) to 0.070 ppm (70 ppb) in conjunction with retaining the indicator (O₃), averaging time (8 hours), and form (4th-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 O₃, 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 O₃ 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 O₃ 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).

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1
2 The 2015 Decision was a public welfare policy judgment made by the Administrator, which drew upon
3 the available scientific evidence for O₃-attributable welfare effects and on analyses of exposures and
4 public welfare risks based on impacts to vegetation, ecosystems and their associated services, as well as
5 judgements about the appropriate weight to place on the range of uncertainties inherent in the evidence
6 and analyses.

7
8 Considerations Regarding Adequacy of the Prior Standard
9

10 The Administrator's conclusion in the 2015 Review regarding the adequacy of the Secondary Standard
11 that was set in 2008 (0.075 ppm, as annual 4th-highest daily maximum 8 hour average concentration
12 averaged over three consecutive years) gave primary consideration to the evidence of growth affects in
13 well-studied tree species and information in cumulative seasonal ozone exposures in certain study areas.
14 In doing so, the exposure information for Class I areas was evaluated in terms of the W126 Cumulative
15 Seasonal Exposure Index, an index recognized by the 2013 ISA as a mathematical approach "for
16 summarizing ambient air quality information in a biologically meaningful form for ozone vegetation
17 effects purposes" (2013 ISA). The EPA focused on the W126 index for this purpose consistent with the
18 evidence of the 2013 ISA and advice from the Clean Air Scientific Advisory Committee (CASAC). The
19 Administrator gave particular weight to analysis with focus on exposures in Class I areas, which are
20 lands that Congress set aside for specific uses intended to provide benefits to the public welfare,
21 including lands that are to be protected so as to conserve the scenic value and the natural vegetation and
22 wildlife within such areas and to leave them unimpaired for the enjoyment of future generations. This
23 emphasis on lands afforded special government protections such as national parks and forests, wildlife
24 refuges, and wilderness areas, some of which are designated as Class I areas under the Clean Air Act,
25 was consistent with a similar emphasis in the 2008 Review of the Standard (73 FR 16485, March 27,
26 2008).

27
28 As noted across past reviews of the Ozone Secondary Standard, Administrator's judgments regarding
29 effects that are adverse to public welfare consider the intended use of the ecological receptors, resources,
30 and ecosystems affected. Thus, in the 2015 Review, the Administrator utilized the median RBL estimate
31 for the studied species as a quantitative tool within a larger framework of considerations pertaining to
32 the public welfare significance of O₃ effects. The Administrator recognized such considerations to
33 include effects that are associated with effects on growth and that the 2013 ISA determined to be
34 causally or likely causally related to ozone and ambient air, yet for which there are greater uncertainties
35 affecting estimates of impacts on public welfare. These other effects included reduced productivity in
36 terrestrial ecosystems, reduced carbon sequestration in terrestrial ecosystems, alteration of terrestrial
37 community composition, alteration of below ground biogeochemical cycles, and alteration of terrestrial
38 ecosystem water cycles. The Administrator in considering the revised lower standard, noted that a
39 revised Standard would provide increased protection for other growth-related effects, including for
40 relative yield loss (RYL) of crops, reduced carbon storage and for types of effects for which it is more

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1 difficult to determine public welfare significance, as well as for other welfare effects of ozone, such as
2 visible foliar injury (80 FR 65390, October 26, 2015).

3
4 In reaching a conclusion in the amount of public welfare protection from the presence of ozone and
5 ambient air that is appropriate to be afforded by a revised Secondary Standard, the Administrator gave
6 particular consideration to the following:

- 7
8 1. The nature and degree of effects of O₃ on vegetation,
9 2. The strength and limitations of the available and relevant information,
10 3. Comments from the public on the Administrator's proposed decision, and
11 4. The CASAC reviews regarding the strength of the evidence and its adequacy to inform
12 judgements on public welfare protection.

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

16
17 Does the Current Evidence Alter Conclusions from the Last Review Regarding the Nature of
18 Welfare Effects Attributable to O₃ in Ambient Air?

19
20 The evidence newly available in this Review supports, sharpens, and expands on the conclusions
21 reached in the last Review (Draft Ozone ISA, Appendices 8 and 9). Consistent with the evidence in
22 the last Review, the currently available evidence describes an array of ozone effects on vegetation
23 and related ecosystem effects as well as the role of ozone in radiative forcing and effects on
24 temperature, precipitation, and related climate variables. Evidence newly available in this review
25 augments more limited previously available evidence related to insect interaction with vegetation,
26 contributing to conclusions regarding ozone effects on plant-insect signaling (Draft Ozone ISA,
27 Appendix 8) and on insect herbivores (Draft Ozone ISA, Appendix 8). Thus, the conclusions
28 reached by EPA in the last Review are supported by the current evidence base and conclusions are
29 reached in a few new areas based on the now expanded evidence. The 2019 Ozone PA details of
30 effects of ozone on vegetation and ecosystem processes are reviewed in detail and updated with
31 newly available evidence.

32
33
34
35 Public Welfare Implications

36
37 The public welfare implications of the evidence regarding ozone welfare effects are dependent on
38 the type and severity of the effects, as well as the extent of the effect at a particular biological or
39 ecological level of organization. In the Draft Ozone PA, EPA discusses such factors in light of
40 judgements and conclusions made in prior reviews regarding effects on the public welfare. As

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1 provided in Section 109 (b) (2) of the Clean Air Act, the Secondary Standard is to “specify a level of
2 air quality the attainment and maintenance of which in the judgement of the Administrator...is
3 requisite to protect the public welfare from any known or anticipated adverse effects associated with
4 the presence of such air pollutant in the ambient air”. The Secondary Standard is not meant to protect
5 against all known or anticipated ozone related welfare effects, but rather those that are judged to be
6 adverse to the public welfare in a bright line determination of adversity it is not required in judging
7 what is requisite. Thus, the level of protection from known or anticipated adverse effects to public
8 welfare that is requisite for the Secondary Standard is a public welfare policy judgement to be made
9 by the Administrator.

10
11 Is There Information Newly Available in this Review Relevant to Consideration of the Public
12 Welfare Implications of Ozone Related Welfare Effects?

13
14 The categories of effects identified in the Clean Air Act to be included among welfare effects are
15 quite diverse and, among these categories, any single category includes many different types of
16 effects that are of broadly varying specificity and level of resolution. For instance, effects on
17 vegetation is a category identified in the Clean Air Act Section 302 (h), and the 2019 Ozone ISA
18 recognized numerous vegetation related effects of ozone at the organism, population, community,
19 and ecosystem level (Draft ISA, Appendix 8). In the decisions to revise the Secondary Standard in
20 the last two reviews (2008, 2015) the Administrator recognized that by providing protection based
21 on consideration of effects in natural ecosystems in areas afforded special protection, the revised
22 Secondary Standard would also “provide a level of protection for other vegetation that is used by the
23 public and potentially affected by ozone including timber, produce grown for consumption and
24 horticultural plants used for landscaping” (80 FR 65403, October 26, 2015). EPA provides in the
25 Ozone PA figure 4-2. Potential effects of O₃ on the public welfare, which does an excellent job at
26 summarizing the potential effects of causal or likely to be causal impact of ozone on vegetation at
27 the organism, population, community, and ecosystems levels.

28
29 Exposures Associated with Effects

30
31 The types of effects identified in Figure 4-2 of the Ozone PA vary widely with regard to the extent
32 and level of detail of the available information that describes the ozone exposure circumstances that
33 may elicit them. Therefore, EPA organized a section in the 2019 Ozone PA to address first, effects
34 of ozone exposure on growth and yield effects, a category of effects for which information on
35 exposure metrics and E-R relationships is most advanced. In addition, EPA discusses the current
36 information available regarding exposure metrics and relationships between exposure and the
37 occurrence and severity of visible foliar injury.

38
39 Growth Related Effects

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1 The longstanding body of vegetation effects evidence includes a wealth of information on
2 aspects of ozone exposure that are important in influencing effects on plant growth and yield
3 (Draft 2019 ISA). A variety of factors have been investigated, including “concentration, time of
4 day, respite time, frequency of peak occurrence, plant phenology, predisposition, etc.” (2013
5 Ozone ISA). In the last several reviews, based on the then available evidence, as well as advice
6 from the CASAC, the EPA has focused on the use of cumulative, seasonal concentration-
7 weighted index for considering the growth related effects evidence and in quantitative exposure
8 analyses for purposes of reaching conclusions on the Secondary Standard. More specifically, the
9 EPA used the W126-based cumulative, seasonal metric (Draft 2019 ISA). This metric,
10 commonly called the W126 Index, is a non-threshold approach described as the sigmoidally
11 weighted sum of all hourly ozone concentrations observed during a specified daily and seasonal
12 time window, where each hourly ozone concentration is given a weight that increased from 0-1
13 within increasing concentration (2013 ISA). The most well studied data sets in this regard are
14 those for 11 tree species seedlings and ten crops referenced and described by Lee and Hogsett
15 (1996) and Hogsett et al (1997). These datasets include 1) for growth effects on seedlings of a set
16 of tree species and 2) for quality and yield effects of a set of crops. These datasets, which include
17 growth and yield response information across a range of multiple seasonal cumulative exposures,
18 were used to develop robust, quantitative, E-R functions for reduced growth (termed Relative
19 Biomass Loss or RBL). In seedlings of the tree species and E-R functions for RYL for a set of
20 common crops (Draft 2019 ISA, Appendix 8) the EPA’s conclusions regarding exposure levels
21 of ozone associated with vegetation related effects at the time of the last review were based
22 primarily on these established E-R functions. The 2019 Ozone Draft ISA concludes that “the
23 cumulative exposure indices, including the W126 Index, “are the best available approach for
24 studying the effects of ozone exposure on the vegetation in the U.S.” (Draft 2019 Ozone ISA,
25 Appendix 8). Accordingly, in this review, the EPA as in the last two reviews used the seasonal
26 W126-based cumulative, concentration-weighted metric for consideration of the effects evidence
27 in quantitative exposure analyses, particularly related to growth effects, which appears
28 reasonable and scientifically sound. This information for the tree species, in combination with air
29 quality analysis was a key consideration in the 2015 EPA decision on the level for the revised
30 Secondary Standard (80 FR 65292, October 26, 2015).

31
32 Other Effects

33
34 With regard to climate related effects, including radiative forcing, the newly available evidence
35 in this review does not provide more detailed quantitative information regarding ozone
36 concentrations at the national scale. Although ozone continues to be recognized as having a
37 causal relationship with radiative forcing and a likely causal relationship with effects on
38 temperature, precipitation, and related climate variables, the non-uniform distribution of ozone
39 (spatially and temporally) makes the development of quantitative relationships between the
40 magnitude of such effects in differing ozone concentrations in the U.S. challenging (Draft 2019

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1 Ozone ISA, Appendix 9). Thus, the Draft 2019 Ozone ISA recognizes that “current limitations in
2 climate modeling tools, variation across models, and the need for more comprehensive
3 observational data on these effects represents sources of uncertainty in quantifying the precise
4 magnitude of climate responses to ozone changes, particularly at regional scales (Draft 2019
5 Ozone ISA). While these complexities affect EPA’s ability to consider specific ozone
6 concentrations associated with differing magnitudes of climate-related effects, it does give EPA
7 the ability to estimate growth-related impacts of trees that can inform their consideration of the
8 sequestration of carbon in terrestrial ecosystems, a process that can reduce tropospheric
9 abundance of the pollutant (CO₂) ranked first in importance as a greenhouse gas and radiative
10 forcing agent.

11
12 What Are Important Uncertainties in the Evidence?

13
14 Among the categories of effects identified in past reviews, key uncertainties remain in the current
15 evidence (Draft Ozone PA 2019). The category of ozone welfare effects for which current
16 understanding of quantitative relationships is strongest is reduced plant growth. As a result, this
17 category was the focus of the Administrator’s decision making in the last review, with RBL in tree
18 seedlings playing the role of surrogate for the broader array of vegetation related effects that range
19 from the individual plant level to ecosystem services. Limitations in the evidence base and
20 associated uncertainties recognized in the last review remain and include a number of uncertainties
21 that affect characterization of the magnitude of cumulative exposure conditions eliciting growth
22 reductions in U.S. forests.

23
24 As recognized in the last review, there are uncertainties in the extent to which the 11 tree species for
25 which there are established E-R functions encompass the range of ozone sensitive species in the U.S.
26 and also the extent to which they represent U.S. vegetation as a whole. Therefore, it should not be
27 assumed that species of unknown sensitivity are tolerant to ozone.

28
29 EPA recognized important uncertainties in extent to which the E-R functions for reduced growth in
30 tree seedlings are also descriptive of such relationships during later life stages for which there is a
31 paucity of established E-R relationships. In addition, EPA recognizes limitations and their ability to
32 estimate growth effects of tree lifetimes of year to year variation in ozone concentrations. For
33 example, the studies on which the established E-R functions for 11 tree species are based vary in
34 duration (such as 82 days in a single year to 555 days spanning more than one year). In the 2019
35 Draft Ozone PA, EPA goes to great lengths in walking through uncertainties and recognizing
36 limitations and data interpretation with a number of studies that they have considered. This is not
37 unexpected due to the biological variability in response to a pollutant such as ozone in ecological
38 systems.

39 Exposure and Air Quality Information

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

7
8 In revising the Standard in 2015 to the now current Standard, the Administrator concluded that with
9 revision of the Standard level, the existing form and averaging time provided the control needed to
10 achieve the cumulative seasonal exposure circumstances identified for the Secondary Standard. The
11 focus of cumulative seasonal exposure primarily reflects the evidence of E-R relationships for plant
12 growth. The 2015 conclusion was supported by the air quality data analyzed at that time. Analysis in
13 the 2019 current review of the still more expanded set of air monitoring data, which includes 1,545
14 monitoring sites with sufficient data for variation of design values, documents similar findings as
15 from the analysis of data from 2000 -2013 described in the last review.

16
17 Monitoring sites with lower ozone concentrations as measured by the design value metric (based on
18 the current form and averaging time of the Secondary Standard) also have lower cumulative seasonal
19 exposures, as quantified by the W126 Index. As the form and averaging time of the Secondary
20 Standard have not changed since 1997, the analyses performed have been able to assess the control
21 exerted by these aspects of the standard in combinations with reductions in the level (i.e., from 80
22 ppb in 1997 to 75 ppb in 2008 to 70 ppb in 2015) on cumulative seasonal exposures in terms of the
23 W126 Index.

24
25 In the 2019 Draft Ozone PA in Figure 4-7, W126 Index values at monitoring sites with valid design
26 values (2015-2017) the evidence currently available leads EPA to conclusions regarding exposure
27 levels associated with effects as similar conclusions in the last review. Based largely on this
28 evidence in combination with use of RBL as a surrogate, for vegetation related effects, the value of
29 17 ppm-hrs was the average W126 Index (over three years) was identified in the 2015 decision (80
30 FR 65393; October 26, 2015). As summarized above, the information available in the present review
31 continues to indicate that cumulative seasonal exposure levels at virtually all sites with air quality
32 meeting the current standard fall below the level of 17 ppm-hrs that was identified when the current
33 standard was established (80 FR 65393; October 26, 2015). Additionally, the average W126 Index in
34 Class I areas that meet the current standard for the most recent three year period is below 17 and at
35 or below 13 ppm-hrs in 44 of those of 46 Class I areas. In addition, in the current draft 2019 Ozone
36 PA, table 4-2 summarizes distribution of W126 Index values in/near Class I areas. In summary, as is
37 the case at all monitoring sites nationally, sites in or near Class I areas with design values at or below
38 70 ppb in the most recent three year period have had a seasonal W126 Index (based on three year
39 average) at or below 17 ppm-hrs. As was the case at the time the current standard was established,
40 with the exception of four values that occurred nearly a decade ago in the southwest region,

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1 cumulative seasonal exposures in all Class I areas during periods that met the current standard were
2 no higher than 17 ppm-hrs which reflects a protective level in the standard.

3
4 Based on established E-R functions for tree seedling growth reductions in 11 species, the tree
5 seedling RBL for the median tree species is 5.3% for a W126 Index of 17 ppm-hrs, rising to 5.7%
6 for 18 ppm-hrs, 6% for 19 ppm-hrs and 6.4% for 20 ppm-hrs. Below 17 ppm-hrs, median estimates
7 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.
8 These estimates are unchanged from what was indicated by the evidence in the last review.

9
10 EPA has focused in the current review on the E-R relationships available in the last review for
11 purposes of considering ozone exposure levels associated with growth-related impacts. Currently
12 available evidence, including the newly available in the 2019 Ozone Draft ISA does not indicate the
13 occurrence of ozone-related effects attributable to cumulative ozone exposures lower than was
14 established at the time of the last review (.07 ppm). As in the last review, the currently available
15 evidence continues to support a cumulative, seasonal exposure index as a biologically-relevant and
16 appropriate metric for assessment of the evidence of exposure/risk information for vegetation, most
17 particularly for growth related effects. This is reasonable, responsible, and reflects good use of
18 scientific information by the EPA. The evidence continues to support important roles for cumulative
19 exposure and for weighting higher concentrations over lower concentrations of ozone and ambient
20 air. Thus, among the various such indices considered in the literature the cumulative, concentration-
21 weighted W126 function continues to be best supported for purposes of relating ozone air quality to
22 growth-related effects.

23
24 The RBL appears to be appropriately considered as a surrogate for an array of adverse welfare
25 effects and based on consideration of ecosystem services and potential for impacts to the public as
26 well as conceptual relationships between vegetation growth effects and ecosystem scale effects.
27 Biomass loss is a scientifically sound surrogate of a variety of adverse effects that could be exerted
28 to public welfare. In the previous review, the Administrator used RBL as a surrogate for
29 consideration of the broader array of vegetation related effects of potential welfare significance that
30 included effects of growth of individual sensitive species and extended to ecosystem level effects
31 such as community composition in natural forests, particularly in protected public lands (80 FR
32 65406, October 26, 2015). EPA believes, and I concur, that information available in the present
33 review does not call into question this approach, indicating there continues to be support for the use
34 of tree seedling RBL as a proxy for the broader array of vegetation-related effects, most particularly
35 those related to growth.

36
37 To What Extend Does the Available Information Alter Our Understanding of the Magnitude of
38 Growth Reductions Expected to be of Public Welfare Significance?
39

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1 It was recommended in the last review that a 6% RBL was “unacceptably high” and endeavored to
2 identify a Secondary Standard that would limit three year average ozone exposures somewhat below
3 W126 Index values associated with a 6% RBL in the median species. This led to identification of a
4 seasonal W126 Index value of 17 ppm-hrs that the Administrator concluded appropriate as a target at
5 or below which the new Standard would generally restrict cumulative seasonal exposures (80 FR
6 65407, October 26, 2015). The currently available evidence continues to indicate conceptual
7 relationships between reduced growth and the broader array of vegetation-related effects of ambient
8 ozone exposure.
9

10 What Does the Information Available in the Current Review Indicate with Regards to Support for
11 Use of a Three Year Average Seasonal W126 Index as the Cumulative Exposure Metric (Associated
12 with a Value of 17 ppm-hrs) for Describing the Requisite Level of Protection for the Secondary
13 Standard?
14

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

28 Does the Currently Available Scientific Evidence in Air Quality and Exposure Analyses Support or
29 Call into Question the Adequacy of the Protection Afforded by the Current Secondary Ozone
30 Standard?
31

32 As delineated by the Clean Air Act, the Secondary Standard is meant to protect against ozone related
33 welfare effects that are judged to be adverse to the public welfare. The EPA in development of the
34 Draft 2019 Ozone PA considered the currently available information regarding welfare effects of
35 ozone in this context, while recognizing that the level of protection from known or anticipated
36 adverse effects to public welfare that is requisite for the Secondary Standard is a public welfare
37 policy judgement made by the Administrator. EPA considered the quantitative analyses, including
38 associated limitations and uncertainties and the extent to which they indicate differing conclusions
39 regarding the level of protection indicated to be provided by the current Standard from adverse
40 effects. EPA additionally considered the key aspects of the evidence in air quality/exposure

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1 information emphasized in establishing the now current Standard and the associated public welfare
2 policy judgements and judgements about inherent uncertainties that are integral to decisions on the
3 adequacy of the current Secondary Ozone Standard. In considering the currently available evidence,
4 EPA recognized the long-standing evidence base of the vegetation-related effects of ozone,
5 augmented in some aspects since the last review. Consistent with the evidence in the last review, the
6 currently available evidence describes an array of ozone effects on vegetation and related ecosystem
7 effects as well as the role of ozone in radiative forcing with effects on climate related variables. The
8 current evidence base supports conclusions of causal relationships between, particularly, vegetation
9 and other endpoints and likely to be causal relationships between other endpoints that EPA
10 thoroughly discussed in the 2019 Draft ISA. EPA appropriately recognized uncertainties in
11 categories of effects newly identified that could limit consideration of the protection that might be
12 provided by the current Standard against these effects.

13
14 As was the case in the last review, a category of effects for which the evidence supports quantitative
15 description of relationships between air quality conditions and response is plant growth or yield. The
16 evidence base continues to indicate growth-related effects as sensitive welfare effects, with the
17 potential for ecosystem scale ramifications. For this category of effects, there are established E-R
18 functions that relate cumulative seasonal exposure of varying magnitudes to various incremental
19 reductions in expected tree seedling growth (in terms of RBL) and in expected crop yield. Decades
20 of research also recognizes visible foliar injury as an effect of ozone, although uncertainties continue
21 to hamper efforts to quantitatively characterize the relationship of its occurrence and relative severity
22 with ozone exposures.

23
24 Reviews of NAAQS also required judgements on the extent to which particular welfare effects (such
25 as with regard to type, magnitude/severity, or extend) are important from a public welfare
26 perspective. In the case of ozone, such a judgement includes consideration of the public welfare
27 significance of small estimates of RBL and associated unquantified potential for larger scale effects.
28 With regard to public welfare significance of 5-6% RBL, the EPA notes CASAC characterization of
29 6% RBL (in seedlings of median tree species) in the last review. The rationale provided by the
30 CASAC with this characterization was primarily conceptual and qualitative rather than quantitative.
31 The conceptual characterization recognized linkages between effects on the plant level scale and
32 broader ecosystem impacts, and this facilitated the Administrator consider RBL as a surrogate for
33 the broader impacts that could be elicited by ozone. In the 2015 decision, the Administrator took
34 note of CASAC advice regarding use of RBL as a proxy and set the Standard with “underlying
35 objective of a revised Secondary Standard that would limit cumulative exposures in nearly all
36 instances to those for which the median RBL estimate would be somewhat lower than 6%” (80 FR
37 65407, October 26, 2015). The 2015 decision noted that “the Administrator does not judge RBL
38 estimates associated with marginal higher exposures [at or above 19 ppm-hrs] in isolated rare
39 instances to be indicative of adverse effects to the public welfare” (80 FR 65407, October 26, 2015).

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1 In considering the quantitative analyses available in the draft 2019 Ozone PA, EPA noted the
2 findings from the analysis of recent air quality at sites across the U.S., including in or near 64 Class I
3 areas and also analysis of historical air quality. Findings from the analysis of air quality data from
4 the most recent period and from the larger analysis of historical air quality data extended back to
5 2000 are consistent with the air quality analysis findings that were part of the basis for the current
6 Standard. That is, in virtually all design value periods and in all locations at which the current
7 Standard was met, the three year average W126 metric was at or below 17 ppm-hrs, the target
8 identified by the Administrator in establishing the current Standard (80 FR 65404-65410, October
9 26, 2015).

10
11 EPA summarized in the draft 2019 Ozone PA there is little in the information available in the current
12 review that differs from that in the last review that relate to key aspects of the judgments and
13 associated decision that established the current Standard in 2015. The new information available is
14 consistent with that available in the last review for the principle effects for which the evidence is
15 strongest (such as growth, reproduction, and related larger scale effects, as well as visible foliar
16 injury).

17
18 General Comments

- 19
20 1. I compliment the United States Environmental Protection Agency on a very thorough and well-
21 written Chapter 4 contributing to the draft 2019 Ozone Policy Assessment.
- 22 2. The foundation upon which scientific data was utilized while also incorporating concepts of
23 judgement on behalf of the EPA with input from various entities lays a strong and clear scientific
24 process of considerations for the preliminary conclusions on the current Secondary Standard.
- 25 3. The preliminary conclusion by the U.S. EPA that the 2015 decision to revise the level of the
26 Secondary Standard for photochemical oxidants, including ozone to .07 ppm (70 ppb) in
27 conjunction with retaining the indicator (O₃), averaging time (8 hours) and form (4th highest
28 annual daily maximum 8-hour average concentration, averaged across three years) appears to be
29 working in maintaining ambient air concentrations of ozone across the United States at levels
30 that are protective for the public welfare, particularly as related to vegetation.
- 31 4. EPA recommends the RBL appears to be appropriately considered as a surrogate for an array of
32 adverse welfare effects and based on consideration of ecosystem services and potential for
33 impact to the public as well as conceptual relationships between vegetation growth effects and
34 ecosystem scale effects. I agree that biomass loss, as reported in RBL, is a scientifically sound
35 surrogate of a variety of adverse effects that could be exerted to public welfare.
- 36 5. EPA believes, and I concur, that information available in the present review does not call in to
37 question this RBL approach, indicating there continues to be support for the use of tree seedling
38 RBL as a proxy for the broader array of vegetation related effects, most particularly those related
39 to growth that could be impacted by ozone.

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 - 12
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.

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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 NO_x 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

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1 described in the paragraph following this sentence, and so this initial statement needs to be changed to
2 more accurately reflect that.

3
4 In section 3.3.1.1 the EPA states that “Evidence regarding respiratory infections and associated effects
5 has been augmented by a number of epidemiologic studies reporting positive associations between
6 short-term O₃ concentrations and emergency department visits for a variety of respiratory infection
7 endpoints (draft ISA, Appendix 3, section 3.1.7.4).” Section 3.1.7.4 of the ISA also shows a number of
8 studies that do not report positive associations between ozone and infections - the EPA needs to consider
9 how to report these and other epidemiology results in a more balanced manner.

10
11 Fully Justified Conclusions

12
13 There are a few places in this document that require some editing to ensure that the EPA has fully
14 supported the conclusions that are being drawn.

15
16 In section 3.3.1.2 (Other Effects), the EPA does not adequately explain why the evidence for metabolic
17 effects is likely causal, when they state that the data is mostly from animal studies with high exposure
18 levels and there is limited concordance with human epidemiology studies with some contradictory
19 evidence. Similar with long-term exposure and metabolic effects.

20
21 In section 3.3.3, the EPA notes in reference to experimental animal results of respiratory effects that
22 “The exposures eliciting the effects in these studies included multiple 5-day periods with O₃
23 concentrations of 500 ppb over 8-hours per day (draft ISA, section 3.2.4.1.2).” This type of information
24 should be considered for biological plausibility, not just when deciding on relevant concentrations for
25 risk assessment.

26
27 Additional Policy-Relevant Information

28
29 There are some areas where additional information could be added to help provide information to
30 decision makers. In Section 3.3.2 the EPA could add what fraction of the population (particularly at-risk
31 populations if possible) are expected to spend 6.6 hours or more outdoors at moderate exertion. This
32 information would help decision makers compare the exposure likelihood to the primary CHE studies.

33
34 In section 3.5.1 (Evidence-based considerations) the EPA notes that “The current evidence does not alter
35 our understanding of populations at risk from health effects of O₃ exposures.” However, what about the
36 new metabolism causality determination? Does this suggest that people who are obese or have metabolic
37 syndrome are more susceptible?

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1 Study Limitations
2

3 In section 3.3.3 the EPA states that “We have also considered what may be indicated by the
4 epidemiologic studies regarding exposure concentrations associated with health effects, and particularly
5 by such concentrations that might occur in locations when the current standard is met. In so doing,
6 however, we recognize that these studies are generally focused on investigating the existence of a
7 relationship between O₃ occurring in ambient air and specific health outcomes, and not on detailing the
8 specific exposure circumstances eliciting such effects” And “these studies generally do not measure
9 personal exposures of the study population or track individuals in the population with a defined
10 exposure to O₃ alone. Notwithstanding this, we have considered the epidemiologic studies identified in
11 the draft ISA as to what they might indicate regarding O₃ exposure concentrations in this regard.” It is
12 good that the EPA acknowledged this limitation with these studies. Consistent with the
13 recommendations from the expert consultants, these caveats should be applied to all similar air pollution
14 epidemiology studies, not just those for ozone.
15

16 Clarity of Presentation
17

18 There are a few places in this document that require some editing to ensure that data and analyses are
19 clearly reported.
20

21 In section 3.4.2 (Population Exposure and Risk Estimates for Air Quality Just Meeting the Current
22 Standard) and elsewhere the EPA refers to the population exposure estimates (i.e. the estimates of
23 percent of the population exposed to certain concentrations of ozone) as a risk estimate. On its surface,
24 these estimates appear to be exposure, rather than risk, estimates. The EPA should clarify their
25 definitions of risk and exposure for readers.
26

27 The EPA presents quite different risk estimates from the MSS and E-R models. These are discussed at
28 length in Appendix 3D, with an in-depth justification of the choice of the E-R model risk results over the
29 MSS results. The EPA should add more of this information to the main text to clarify further to the
30 reader why they emphasize the E-R model results over the MSS results.
31

32 The EPA states that “The limited evidence that informs our understanding of potential risk to people
33 with asthma is uncertain but indicates the potential for them to experience greater effects or have lesser
34 reserve to protect against such effects than other population groups under similar exposure
35 circumstances, as summarized in section 3.3.4 above.” It is not the case that the limited evidence
36 indicates the potential for people with asthma to experience greater effects, although it is true and logical
37 that they may have less reserve. These two aspects need to be discussed separately and the differences
38 noted, because the ways in which they are taken into account are different. For the former, you assume
39 that people with asthma have a steeper E-R response, or a lower threshold (although there is little data to

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1 suggest that this is the case). For the latter, you use a lower adverse effect threshold, as the EPA already
2 does with the 10% FEV1 decrement threshold.

3
4 In section 3.4.5 (Public Health Implications), I suggest adding a summary of the percent of children with
5 asthma experiencing a 10% FEV1 decrement, with a sentence or two about the adversity of those
6 changes in lung function.

7
8 Quantitative Uncertainty Analysis
9

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

19
20 The EPA discusses uncertainties with air quality analysis in section 3.4.4 (Key Uncertainties) as well as
21 the ways in which they have tried to reduce this uncertainty. However, this type of uncertainty is a prime
22 candidate for a quantitative uncertainty analysis because there are estimates on the uncertainties
23 associated with the air quality estimates.

24
25 In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that “In recognition of the lack of data for
26 some at risk groups and the potential for such groups, such as children with asthma, to experience lung
27 function decrements at lower exposures than healthy adults, both models generate nonzero predictions
28 for 7-hour concentrations below the 6.6-hour concentrations investigated in the controlled human
29 exposure studies.” The EPA should provide a rationale for assuming a lack of threshold in an exposure-
30 response relationship as a way of considering potential at-risk populations that may not have been
31 characterized in an exposure-response assessment. As per the expert consultant responses it is not clear
32 that this is a validated assumption for models based on CHE study data.

33
34 Risk Threshold
35

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

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1 concept of threshold should be discussed by EPA in the main text and should be considered as a factor
2 that is incorporated into the E-R model.

3
4 Other Notes

5
6 In the Appendices in a number of locations there is “Error Reference Not Found!” - these need to be
7 located and fixed.

8
9 In section 3.3.1.1 Footnote: “As recognized in section 3.3.1.1 above, the single newly available 6.6-hour
10 study is for subjects aged 55 years of age or older, and has a slightly lower target ventilation rate for the
11 exercise periods. The exposure concentrations were 120 ppb and 70 ppb, only the former of which
12 elicited a statistically significant FEV1 decrement in this age group of subjects (draft ISA, Appendix 3,
13 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
14 hour exposure.

15
16 The end of the second bullet point on page 3-51 is cut-off mid sentence.

17
18 The last sentence of the first paragraph on page 3-82 needs to be edited - there seem to be words missing
19 or juxtaposed.

20
21 There is a figure (referenced in page 3D-91) that seems to be labeled as “0”, instead of with the figure
22 name.

23
24 Questions to Consultants

25
26 *1) Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have*
27 *demonstrated that in an area where peak daily ozone concentrations have decreased over time,*
28 *over the same period of time the lowest daily ozone concentrations have also decreased (due to*
29 *the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are*
30 *your thoughts about the change of annual average ozone concentrations (which tend to be the*
31 *focus of epidemiology studies) with decreases in annual peak ozone concentrations?*
32

33 Responses:

34
35 Dr. Jaffe: “Yes, I agree with your statements: Annual averages have changed much less than the design
36 values due to the NOx disbenefit. How this impacts health is a question for epidemiologists, so I am not
37 able to answer.”
38

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1 Dr. Jansen: “While there may be exceptions, I would expect any changes in the annual averages to be
2 small and could go in either direction. One question I would ask is what the epidemiological studies do
3 when the monitors do not operate for the full year, which is the case of most monitors.”
4

5 Dr. Lipfert: “I used the data for two frequency distributions from Figure 1 to estimate how cumulative
6 risks could depend on the exposure-response function (ERF) threshold. I postulated a linear ERF so that
7 the contribution to the total risk is the product of the frequency and the midpoint of the O₃ concentration
8 bin (Figure 2). With no threshold or up to about 30 ppb, there is no difference in cumulative risk, as is
9 the case with high thresholds (> 80 ppb). In the mid-range (thresholds from 40-80 ppb), the cumulative
10 risk for the higher design value (DV) distribution is about double that of the lower one while the ratio of
11 the 2 DVs is only 1.3, showing the importance of thresholds. Most epi studies have used some measure
12 of peak O₃ rather than the annual average. My own studies (see Appendix) have used the 95th percentile
13 of the daily O₃ averages.”
14

15 Dr. North: “I fully agree that the decrease in annual average ozone exposure is significant. I continue to
16 have concerns on whether the epidemiological results imply manipulative causality as opposed to
17 association, and I am pleased to read that EPA is not using these epidemiological results but rather
18 basing its recommendations (for the last round and the present one) mainly on human clinical studies.
19 There are still areas of the US, such as the Sacramento area, that have MDA8 levels well above the
20 current standard of 70 ppb. I would like to see CASAC focus on the public health risk in these areas. See
21 my general comments above regarding asthma. There ought to be more research to see if high ozone
22 episodes in Sacramento (and elsewhere in the Central Valley and the Los Angeles to San Diego area)
23 have led to increases in hospital admissions and emergency department visits.”
24

25 Dr. Parrish: “The general situation exemplified in Figure 1 is more or less typical of the temporal
26 evolution of urban ozone concentration distributions, where maximum daily 8-hour average (MDA8)
27 ozone concentrations have decreased, but the minimum MDA8 values have increased. This causes the
28 distribution of MDA8 ozone concentrations to narrow, as shown in the figure. The cause of the increase
29 in the minimum MDA8 ozone concentrations is a reduction in fresh NO emissions in the urban area. The
30 effect of these emissions on days of low photochemical activity is for NO to react with ozone, forming
31 NO₂. Thus, between the early 2001-2003 period and the later 2013-2015 period, on days of low
32 photochemical activity the MDA8 ozone concentrations have increased but the NO₂ concentrations have
33 decreased. Since the mean and median MDA8 have not changed significantly over this time interval, it
34 may well be that the annual average ozone concentrations have not changed much. The possibility that
35 annual average ozone concentrations have not changed, but that NO₂ concentrations have decreased,
36 would be important to consider in the interpretation of epidemiology studies that focus on annual
37 average ozone concentrations.”
38

39 Dr. Sax: “EPA does acknowledge that “Reductions of NO_x emissions are expected to result in a
40 compressed O₃ distribution, relative to current conditions” (Draft Ozone PA, pg. 2-4), and it looks like

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1 that is what is shown in Dr. Lang's Figure 1. As Figure 1 shows, however, this also means that there will
2 be more days that experience somewhat higher ozone concentrations, although potentially no days with
3 levels that exceed very high concentrations. With regards to how these changes should be interpreted for
4 epidemiology studies, I think the larger issue of how ambient levels relate to actual personal exposures
5 of ozone and how this impacts exposure measurement error in the epidemiology studies is a more
6 critical issue. In the PA, EPA acknowledge this important source of uncertainty, and is one reason
7 provided for not conducting the "epidemiology- based" risk assessment."
8

9
10 2) *Is an epidemiology study with higher statistical power (sample size) innately more protected*
11 *against problems of confounding, error, and bias, than an epidemiology study with lower*
12 *statistical power (sample size)?*
13

14 Responses:

15
16 Dr. Jansen: "I am not a statistician but I do not see how it could "protect against" confounding etc.
17 Confounding exists or it doesn't. If one tests for confounding then maybe the higher statistical power
18 allows it to be demonstrated more reliably."
19

20 Dr. Lipfert: "No; sample size only affects random error. Effects of measurement error, incomplete
21 control of confounders, or a miss-specified model are independent of sample size. Cohort analyses are
22 widely regarded as the best approach to studying long-term effects, but cohort sample size can only be
23 increased by recruiting more subjects or extending follow-up time, which entails aging and loss of the
24 more susceptible subjects."
25

26 Dr. North: "No. I responded to a similar question in the O3 ISA. Statistical power comes from having a
27 large sample size, and NOT from having resolved issues of confounding, error, and bias. Consider we
28 have a study of 10 million children showing that shoe size predicts reading ability. Because data were
29 obtained from 10 million children, a very large number, the confidence interval is quite narrow. Does
30 this apparently accurate prediction imply that getting children larger shoes will improve their reading
31 ability? No way!"
32

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

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1
2 Dr. Thomas: “No. Sources of selection, information, and confounding biases could potentially affect any
3 study, irrespective of sample size (or power). That said, very large studies conducted by highly
4 experienced investigators generally make every effort to address such problems in the design and
5 analysis and would discuss these issues in their publications. Also, studies of individual-level data may
6 have access to more information to address bias than meta-analyses or aggregate-level studies.”
7
8

9 3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4*
10 *(Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are*
11 *generally assessing the associations between ambient ozone and specific health outcomes and*
12 *are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-*
13 *40¹ and pg 3-43²). Do you think that this statement is correct? If so, is this statement generally*
14 *true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific*
15 *to ozone, then should this caveat always be considered when evaluating exposure concentrations*
16 *associated with these types of epidemiology studies?*
17

18 Responses:

19
20 Dr. Jansen: “Yes, I believe those statements to be correct. I believe the statements are generally true and
21 the caveat should apply generally, not to just ozone. I suspect the reason it is highlighted here in the
22 ozone proceeding is because ozone concentrations may be more variable than, say, PM among micro-
23 environments. Exposure is very dependent on the integrated levels of ozone in those micro-
24 environments, thus the use of the highly complex and data intensive APEX model. That said, it is not
25 clear that why similar efforts are not done for PM and the other NAAQS. Studies have shown
26 differences in PM and their species between the ambient and homes, restaurants, groceries, etc. In many
27 cases PM is higher indoors due to numerous sources (e.g., cooking, dust, pet dander). Note that indoor

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.”

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1 sources of ozone (e.g., air purifiers) were explicitly excluded in this assessment. I find it curious that
2 EPA expends so much effort with APEX on ozone and not PM. Finally, the whole APEX discussion
3 implies but does not demonstrate that the complexities added to APEX result in a more accurate
4 exposure estimate.”

5
6 Dr. Lipfert: “Yes, this is correct in all cases. Epidemiology deals only in numbers, not rationales.
7 Reduced lung function may lead to hospitalization and then to death, but individual longitudinal
8 analyses would be required to follow such a path. Each of these processes would require its own long-
9 term analysis with its own confounders to be controlled and it is possible, perhaps likely, that different
10 pollutants could be involved in each process (except for smoking). I know of no epidemiology studies
11 that link sequential long-term effects. The time-series model of Murray and colleagues (see Appendix)
12 postulates a frail subpopulation from which all daily deaths emanate in response to spikes in air
13 pollution and/or temperature. An advanced version of this model solves for prior relationships with air
14 pollution or temperature but the corresponding time scales are uncertain. This model decouples the
15 causes of frailty from the causes of daily mortality which are likely to differ. Studies of daily mortality
16 and hospital admissions have indicated similar relationships with ozone, but longer-term studies have
17 not.”

18
19 Dr. North: “I am inclined to think that the problem is a general one that will only be resolved by getting
20 data on potential confounders such as income (more generally, socioeconomic status), and extremes of
21 temperature, which have large impacts on mortality and morbidity via mechanisms independent of air
22 pollutants. However, we should understand that at VERY high exposure levels, air pollutants such as
23 ozone and fine particulate matter (e.g., smoke) can cause illness and death. The shape of the exposure-
24 response relationship is critical for assessing the risks. Extrapolation over orders of magnitude is readily
25 done with available mathematics. But how this extrapolation is done should reflect judgment on the
26 biological mechanisms underlying damage to health.”

27
28 Dr. Sax: “I agree with this statement – the ambient data, whether from fixed-site monitors or from
29 modeling data are only surrogates of the actual personal exposures and any differences contribute to
30 exposure measurement errors. This statement is true for all air pollution studies, not only ozone, and this
31 caveat should be included for other air pollution epidemiology studies.”

32
33 Dr. Thomas: “The two statements cited are generally correct and apply broadly to air pollution
34 epidemiology studies, not just ozone. Most epidemiologic studies are based on measurements of ambient
35 pollution levels, which are readily available. For some pollutants, indoor sources or penetration from
36 outdoor sources, local variation in pollutant concentrations, time-activity patterns, etc., can be important
37 sources of inter-individual variation, which some studies have attempted to quantify by, for example,
38 personal monitoring, microenvironmental measurements, exposure modeling, GPS or accelerometer
39 instruments, etc., but such studies are expensive and may be infeasible for large-scale epidemiologic

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1 studies. Since the statements queried do apply to ozone studies, I don't see than any particular caveats
2 are needed to point out the generality of this issue.”
3
4

5 Exposure-Response Modeling
6

7 4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that “In recognition of the lack of*
8 *data for some at risk groups and the potential for such groups, such as children with asthma, to*
9 *experience lung function decrements at lower exposures than healthy adults, both models*
10 *generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations*
11 *investigated in the controlled human exposure studies.” Is assuming a lack of threshold in an*
12 *exposure-response relationship a standard method for considering potential at-risk populations*
13 *that may not have been characterized in an exposure-response assessment?*
14

15 Responses:
16

17 Dr. Lipfert: “I’m not aware of any “standard methods” for dealing with thresholds, aside from controlled
18 (clinical) experiments that are sensitive to selection of subjects. A linear relationship may be the default
19 option with noisy data for which the lowest concentrations may be the least reliable. However, there are
20 good reasons to accept the concept of (essentially) zero threshold, that differ between long- and short-
21 term analyses. The time-series model of Murray and colleagues analyzes daily mortality relationships in
22 terms of the combination of subject frailty and air pollution. Death may result from excess frailty or
23 excess pollution or both. As a result, in a sufficiently large population there will likely always be
24 someone sick enough to succumb to a small air pollution perturbation; the threshold depends on the
25 population at risk. The situation with long-term effects is more complicated. They result from
26 cumulative or repeated exposures after a period of latency, so that effects of pollution abatement will be
27 delayed and it becomes difficult to define the appropriate exposure over the periods involved.
28 Background ozone will also play a role. Here the threshold depends on the characteristics of exposure.
29 Finally, health responses during a year will be the result of both long-and short-term exposures, so that
30 even in the absence of long-term effects there may be pollution-related mortality at any outdoor
31 concentration level. Also, different pollutants may be involved at different time scales.”
32

33 Dr. North: “Yes, assuming a lack of threshold has become a standard method in many areas of EPA’s
34 risk assessment practice. Many of us old-timers believe this practice is questionable, because absence of
35 evidence is not evidence of absence. The biological mechanisms underlying the adverse health response
36 should be assessed based on available information including judgment. Traditional toxicology has used a
37 sigmoid shaped exposure-response function, on the basis that very small exposures (episodic or
38 cumulative) are unlikely to trigger an adverse response but as the exposure increases, the body’s
39 defenses and repair mechanisms can become inadequate, so the adverse effect becomes common in an
40 exposed population. And the response may saturate with most or all of those who are susceptible to it

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1 having the adverse response – e.g., given enough bacteria in the spoiled food, nearly everyone gets sick
2 from eating it. But linearity to zero became common in cancer risk assessment. This assumption was
3 originated as a health-protective default assumption for screening: a plausible upper bound for
4 identifying chemicals deserving more detailed risk analysis, and not for estimating the incidence of
5 human cancer. But linear to zero is often used for the latter purpose.”
6

7 Dr. Sax: “This approach does not make sense to me. If asthmatics are truly more susceptible to the
8 effects of ozone, then it might be that the threshold for effects might be lower, but not zero. Although
9 data are limited, the data that are available do not indicate that asthmatics are more susceptible than non-
10 asthmatics to the effects of ozone. In fact, data are inconsistent, with some studies indicating effects in
11 asthmatics at elevated ozone exposures, but others showing no effects. For example, no effects on lung
12 function were observed in asthmatics compared to non-asthmatics at exposures to 400 ppb for 2 hours
13 (Alexis et al., 2000) and 200 ppb for 2 hours (Mudway et al., 2001).”
14

15 Dr. Thomas: “As I pointed out in earlier rounds of questions, the exact shape of a dose-response
16 relationship at low doses, including the existence or not of a threshold, is difficult if not impossible to
17 determine from feasible-sized epidemiologic studies. Hence, the default analysis model generally
18 assumes low-dose linearity (or log-linearity depending on the form of the outcome variable); see for
19 example the classic paper by Crump, Hoel, Langley, and Peto (1976) I previously cited. This would be
20 true for either main effects in the whole population or for effect modification in potentially sensitive
21 subpopulations, to the extent that the necessary data on individuals are available. The question of effects
22 below the current standard is particularly important, and especially for highly sensitive groups; to the
23 extent that such data exist, any demonstrable low-dose associations should be considered in revising the
24 standard, whether or not the assumption of low-dose linearity or thresholds can be tested.”
25
26

27 5) *The EPA also notes in this section that there is a lack of information about the factors that make*
28 *people more susceptible to ozone-related effects, and that the risk assessment could therefore be*
29 *underestimating the risk. However, the exposure-response model used to estimate the risk of lung*
30 *function decrements uses those people in the health population with a greater response to ozone*
31 *than the mean response (i.e. that fraction of the people in controlled human exposure studies*
32 *who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration*
33 *for more susceptible people in the population?*
34

35 Responses:

36
37 Dr. Lipfert: “Most epidemiology studies assume a homogeneous population at risk which may be
38 convenient but is unrealistic. The remaining life expectancies of those aged 65 and over range from one
39 day to 35 y or more with a median around 15 y. (This situation pertains for populations but not
40 necessarily cohorts, depending on subject selection.) Many air pollution epidemiology studies have

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1 shown higher risks for subjects with pre-existing conditions. Lung cancer mortality rates are
2 proportional to the cumulative cigarettes smoked, even though not all smokers get lung cancer.
3 Following this model, we would expect air pollution-related mortality to respond to cumulative
4 exposures from a few days to decades, depending on many other variables including preexisting disease.
5 The answer to this question is thus: Yes, air pollution epidemiology includes all degrees of susceptibility
6 but the most highly susceptible subjects may dominate the group response.”
7

8 Dr. North: “I am concerned that FEV1 decrements are not a good indicator for adverse health impacts in
9 sensitive populations. (See my general comments at the beginning of this response. FEV1 measurements
10 vary a good deal. The Belzer-Lewis paper mentioned in my O3 ISA response has perceptive criticism
11 about using FEV1 data in research.) It seems to me that lack of information, referring to the words you
12 use in your first sentence, (1) should motivate detailed studies of the people that are judged to be at
13 highest risk, and (2) leaders of agencies such as EPA should think beyond legally required standard
14 setting to the bigger issue of how to protect public health with an adequate margin of safety. If adverse
15 health effects are judged to be essentially absent for much of the United States (a reasonable inference
16 from Figure ES-1 in the ISA and Figure 2-5, page 2-12 in the PA), then attention should be focused on
17 the remaining areas where such adverse health effects may still be occurring. Are these adverse health
18 impacts really there in these remaining areas, or are our government officials being overly precautionary
19 and protective in setting standards, but ignoring major public health protection needs by assuming that
20 some causes, such as wildfires, are “natural background?” EPA should be using common sense and not
21 be trapped in traditions that violate common sense. The levels of ozone and fine particulate matters that
22 millions of people in California have experienced from wildfire smoke plumes in 2017, 2018, and 2019
23 are far above the NAAQS standards and pose serious health effects, especially to members of sensitive
24 subgroups. Some of these people are among my family, my friends, and my neighbors. The costs
25 involved in reducing these risks to health from wildfire plumes are very large. So are the costs of
26 bringing ozone levels in Sacramento into compliance with a 70 ppb MDA8 standard, even if with
27 wildfire periods are exempted. (In my humble judgment, the former activity makes much more sense
28 than the latter.) EPA staff and CASAC should acknowledge these facts in their written documents, as
29 part of advising the EPA Administrator on strategy with respect to criteria air pollutants. I believe giving
30 such advice is within the legal mandate of CASAC under the Clean Air Act.”
31

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

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1 already represents a very conservative estimation of ozone effects that are likely to be protective of
2 sensitive population groups.”

3
4 Dr. Thomas: “This question appears to relate more to controlled human exposure studies than to
5 epidemiologic studies but does seem to be a reasonable approach for getting a handle on inter-individual
6 variability in susceptibility in that context. Obviously, the slope of an exposure-response relationship in
7 the general population will underestimate risk for more sensitive individuals, or more importantly, for
8 identifiable subgroups. Of course, there are other characteristics than lung function (e.g., genetic
9 variants, age/gender, baseline health status, etc.) that could influence sensitivity of ozone or other
10 pollutants. To the extent that the necessary data are available, most epidemiologic studies have reported
11 variation across quantifiable subgroups, and given EPA’s mandate to provide adequate protection to
12 such groups as well as to the entire population should be taken into consideration in revising standards.”

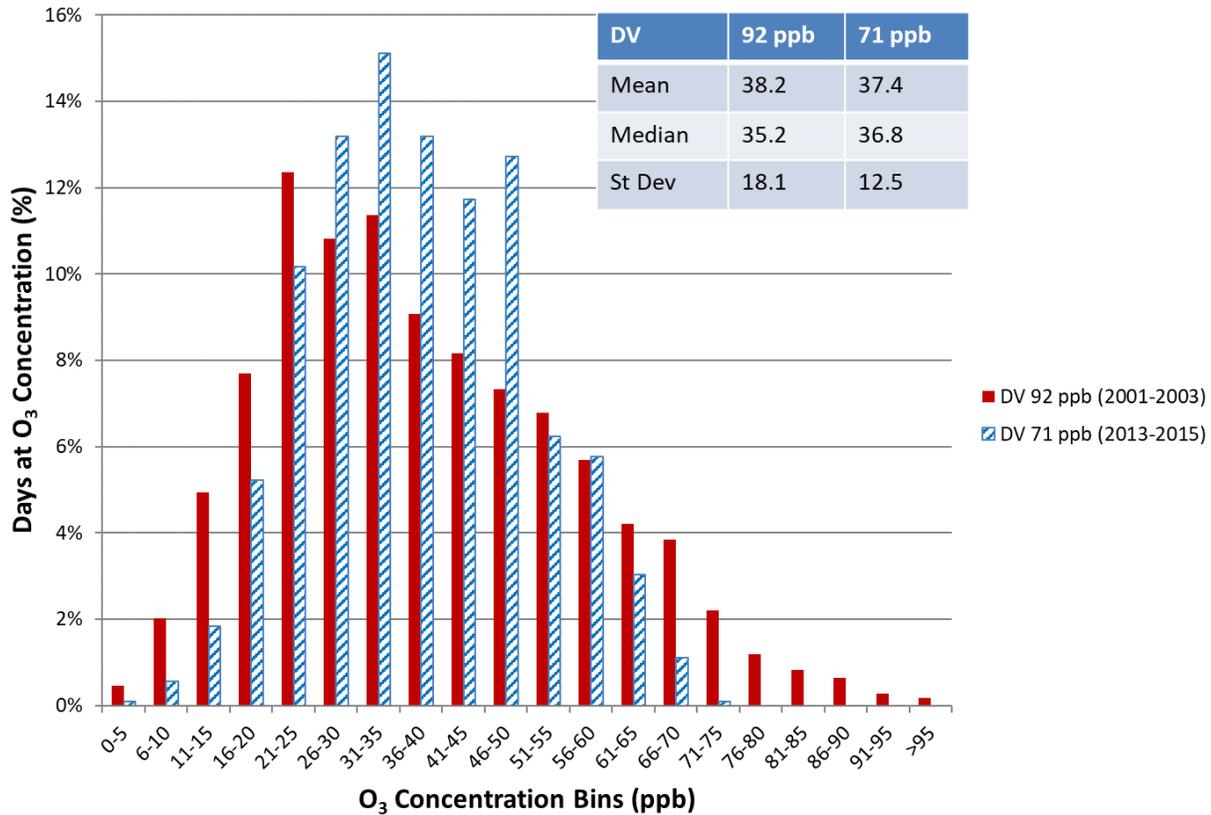
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24
25
26

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St. Louis Mean 8-Hr Max O₃ Concentration at Different Design Values



1
 2 **Figure 1.** Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all
 3 monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV
 4 – design value.
 5
 6
 7

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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 NO_y, 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

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1 This section indicates that otherwise valid epidemiological studies (US and Canada) which found
2 positive associations between ozone and respiratory outcomes were deemed to be less useful since the
3 studies were conducted in areas and during time periods that would not have met the current standard.
4

5 When evaluating epidemiological health effects, should this limitation be placed on study and study
6 result effectiveness? In other words, should epidemiological evidence **only** be limited to those areas that
7 meet the current standard with disregard for effects noted as both higher and lower concentrations that
8 those of the current standard?
9

10 3.4 Exposure and Risk Information

11 General Questions

12 What is the inherent purpose of the risk assessment in the policy assessment evaluation?
13
14 Are the results from the risk assessment viewed to be more substantive than controlled human and
15 epidemiological studies? Even given the extensive list of uncertainties highlighted in 3.4.4
16
17

18 3.4.1 Conceptual Model and Assessment Approach

19
20 For the risk assessment, why the utilization of ambient air monitoring data consisting of concentrations
21 at or near the current standards? Why not consider ozone concentrations well above and below the
22 current standard also?
23

24 3.4.2 Population Exposure and Risk Estimates for Air Quality Just Meeting the Current Standard

25
26 While not totally invalid, some concern with developing risk estimates from concentrations from eight
27 (8) representative cities.
28

29 Greater explanation and concern with ‘simulated children with asthma.’
30

31 While the focus has been on areas just meeting the current standard, how would the percentages change
32 for each benchmark (i.e., 60 ppb, 70 ppb, 80 ppm) for concentrations below the current standard? For
33 concentrations above the current standard?
34

35 3.5.2 Exposure/Risk-Based Considerations

36
37 While not totally invalid, some concern with developing risk estimates from concentrations from eight
38 (8) representative cities.

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1 While the focus has been on areas just meeting the current standard, how would the number of days and
2 lung function decrement changes for concentrations below the current standard? For concentrations
3 above the current standard?
4
5
6
7
8

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1 **Dr. Steven Packham**

2
3 **Preliminary Comment.** Empirical observations and pulmonary function data from controlled
4 human exposures are sufficient to conclude that a causal biological mechanism exists between
5 objectively measured decrements in FEV1 and subjective symptoms in healthy human adults.
6

- 7
1. The shape of the biologically mediated FEV1 dose-response curve is a function of the
8 inhaled hourly dosage rate and the cumulative dose inhaled over several hours
9 immediately prior to the onset of the effect.
 - 10 2. The threshold for these biologically mediated FEV1 responses in healthy adult
11 humans exposed for 6.6 hours to ozone concentrations from 60 to 87 ppb is estimated
12 to be 1,362 µg. (Schelegle et al. 2009)
 - 13 3. This is equivalent to a cumulative dose of millions of trillions of highly reactive oxidizing
14 molecular moieties.
15

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

- 17
- 18 4. The threshold doses for ozone induced FEV1 and reports of symptomatic effects are
19 lower than for clinical signs of pulmonary inflammation.
 - 20 5. Ozone induced FEV1 decrement is most probably one of several specific protective
21 biological responses.
 - 22 6. Ozone exposures have been shown to stimulate peripheral mucus flow into central
23 bronchi thereby enhancing particle transport from peripheral to central airways and
24 mucociliary clearance of inhaled particulate matter.
 - 25 7. This beneficial dose-dependent response to ozone "...is of interest since it
26 characterizes the reaction of a primary defense mechanism essential to the protection
27 of mucosal surfaces of the tracheobronchial tree." (Forster et al. 1987)
28

29 **Recommendations.** In order to present a review of key scientific studies and an integration of
30 current scientific evidence and knowledge, future O3 ISA and PA documents MUST present a
31 clear description of all the known biological mechanisms underlying the O3-FEV1 effect and
32 further validate and refine the dose response functions for FEV1 and pulmonary inflammation
33 derivable from controlled human exposure studies.
34

35
36 In response to the Question,

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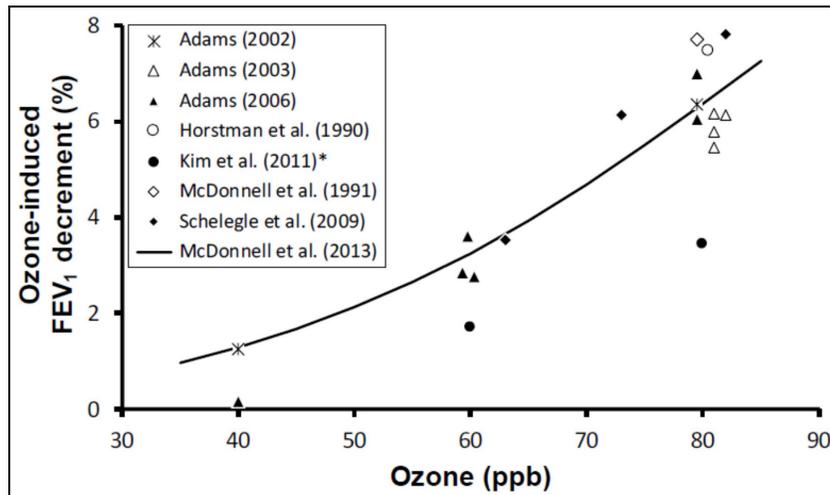
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1 “When a causal relationship is conclusive to a high degree of scientific certainty as it is in this
2 case, should this take precedence over causal inference when drafting a NAAQS ISA?” Dr.

3 Parrish Responded:

4 I have no relevant expertise, so I cannot respond to this question as an expert;
5 however, to a non-expert the answer is obviously, Yes.
6

7 **Substantive-bases for these Recommendations.** Figure ES-3 in the Ozone ISA External
8 Review Draft (shown below) is adapted from the 2013 Ozone ISA which was based on eight
9 human studies published between 1988 and 2013. The 2009 study by Schelegle et al. specifically
10 played a decisive role in the 2015 revision of the O₃ NAAQS from 75 to 70 ppb ([80 FR 65292](#)
11 [Oct 26, 2015](#)).
12

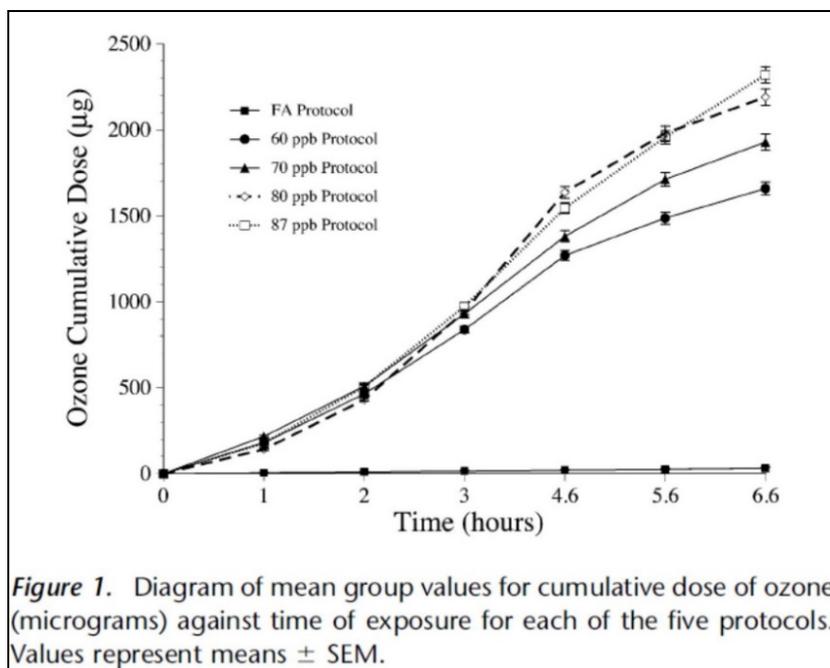


13 **Figure ES-3** was adapted from **Figure 6-1 of 2013 Ozone ISA (U.S. EPA,**
14 **2013)** which was based on studies by Adams (2006), Adams (2003), Adams
15 (2002), Folinsbee et al. (1988), Horstman et al. (1990), Kim et al. (2011),
16 McDonnell et al. (2013), McDonnell et al. (1991), and Schelegle et al. (2009).
17
18

19 In contrast to **Figure ES-3**, the original figure (**Figure 1**) shown below from Schelegle et al.
20 2009, depicts the actual sigmoid curvilinear relationships and mean accumulative doses of the 31
21 healthy adult human subjects who completed the four 6.6-hour chamber exposures to target mean
22 O₃ concentrations of 60,70, 80, and 87 ppb.
23
24

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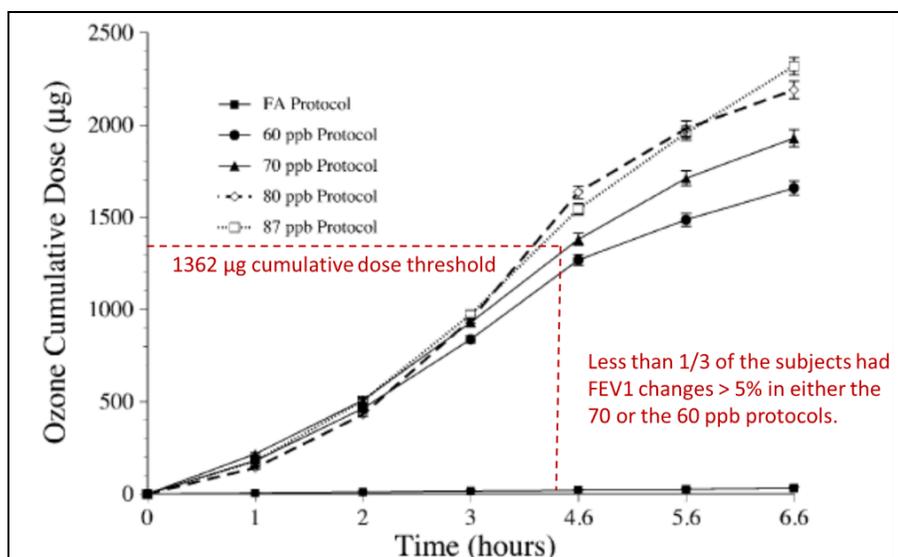


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The original data presented *in this way* conveys critical information to toxicologists and biomedical researchers that is “lost in translation/integration” in the concentration/risk-effect picture presented in Figure ES-3. To quote Schelegle et al. (2009), “*We were able to obtain reliable estimates of a Dose of Onset [i.e., a threshold for the FEV1 effect], using the pooled FEV1 from 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 less than one third of the subjects had changes in FEV1 greater than 5% in either of these protocols.*” (Emphasis added)

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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:

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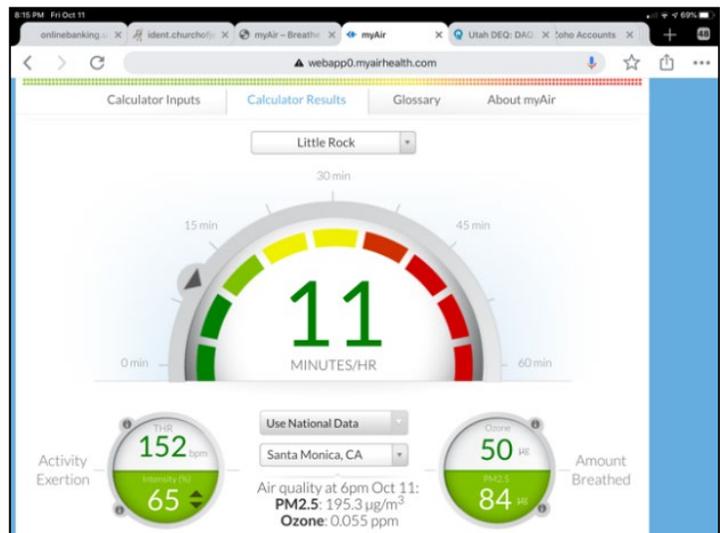
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1 Several nonmember consultants have expressed reluctance to comment on certain questions
2 because of limited familiarity with pulmonary physiology and inhalation toxicology. Here are
3 few facts to keep in mind.

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

12
13 **Overarching Health Benefits from Regulations Based on Sound Science:** An accurate
14 understanding of the causal dose-response relationship between ambient ozone exposure and
15 responses elicited in the human organism opens up a number of important options that could be
16 considered in reviewing and setting NAAQS standards and in how those standards might be used
17 to protect, and even promote, public health. For instance, the realization that the ozone-induced
18 FEV1 effects are temporary, reversible, and occur at a lower inhaled dose than a potential
19 adverse health effect (such as a pulmonary inflammatory response) could be considered a tenable
20 rationale for classifying them as natural benchmark margin-of-safety indicators.

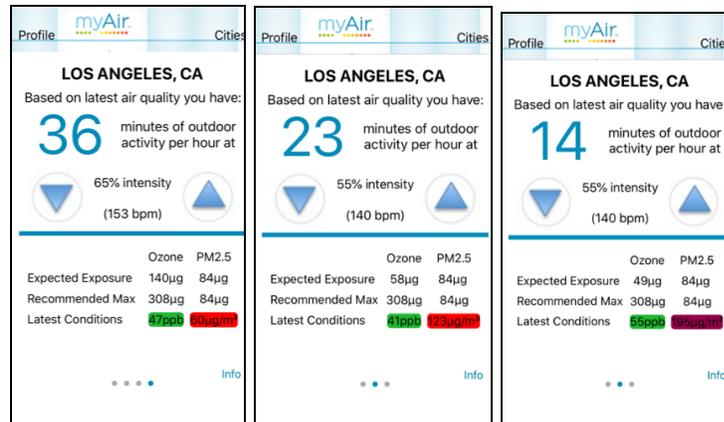
21
22 Another application of minute respiratory volume and hourly MSS inhalation dosage models and
23 thresholds would be for the EPA to imbed
24 them into web and mobile platform
25 applications for public education and personal
26 risk management. Shown here, as proof-of-
27 concept, is a screen shot of such a web
28 application that can be found at
29 <http://webapp0.myairhealth.com/#> giving an
30 individual (user name Little Rock) in Santa
31 Monica California who is being exposed to
32 193 $\mu\text{g}/\text{m}^3$ of PM2.5 on October 11, 2019
33 during the Saddleridge wild fire episode the
34 useful information that they should limit any
35 outdoor activity to 11 minutes or less if that
36 activity necessitates a physical exertion
37 intensity level of 65% corresponding to an
38 average heart rate of 152 beats-per-minute or
39 higher.
40



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1 A free iPhone app is also in the public domain [https://apps.apple.com/us/app/myair-](https://apps.apple.com/us/app/myair-health/id790049340)
2 [health/id790049340](https://apps.apple.com/us/app/myair-health/id790049340). By way of full disclosure, friends and I in Utah developed these web and
3 mobile applications on our own dime and have made them available free to the public since
4 2013. Here are a few screen shots representative of similar guidance being offered to folks in the
5 Los Angeles area during this same Saddleridge fire episode.
6



7
8
9 References to these applications in these comments are not being made to announce, promote, or
10 advocate these particular apps; but, to illustrate the power and potential of using sound scientific
11 methods and fundamental principles of toxicology and human respiratory physiology together
12 with current mobile technology to promote public health and demonstrate the public health value
13 inherent in the EPA O3 and PM NAAQS and their associated Air Quality Index Health
14 Advisories when risk assessment and scientific knowledge from controlled human exposure
15 studies are fully integrated.
16
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18

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10
11
12 **Additional Comments**
13

14
15 COMMENT 1. Evidence of inflammatory markers induced both by exercise and physical exertion (See
16 list of references in EXHIBIT A) should be included in the final Ozone Policy Assessment (O3 PA)
17 along with a discussion of their effects as potential confounders of inflammatory markers associated
18 with ambient ozone exposure.

19
20 COMMENT 2. There needs to be a better presentation of distinctions between a) statistical association
21 versus biological mechanistic concepts of causation, and b) verifiable scientific conclusions versus
22 expert judgments as bases for forming and communicating policy-relevant causal conclusions in the
23 final O3 PA and other documents produced as part of primary NAAQS reviews.

24
25 COMMENT 3. The final O3 PA should include a discussion and analyses of potential benefits of
26 alternative forms of the standard on public health (perhaps in Section 3.1.2.3). There was an intriguing
27 idea presented in public comments by the American Thoracic Society (ATS) suggesting that the form of
28 the standard might be modified to provide better health protection through improved risk
29 communication using the air quality index without changing the stringency of the standard benefits. The
30 final O3 PA should also present a review and a quantitative and qualitative analysis of a) the specific
31 standard form alternatives mentioned in public comments by the ATS, and b) other alternatives in the
32 form of the standard that might reasonably be expected to improve compliance with the standard by
33 increasing the opportunity for states and local air quality agencies in development of adaptive
34 management strategies.

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1 COMMENT 4. The first-time I saw *key* studies used to
2 determine the adequacy of a NAAQS was in 1996.³ In
3 reviewing the three volume PM criteria documentation (CD)
4 as a toxicologist with the Utah Division of Air Quality, I
5 estimated that around 3,885 scientific studies were cited (See
6 TABLE 1). There were at least 390 references on the physical
7 and chemical properties of PM and around 250 references
8 reporting monitoring data of daily and annual background PM
9 concentrations. There were at least 200 references providing
10 data analyses and estimates on human exposure-dose levels
11 and about 500 references on dosimetry and an estimated 500
12 studies on the toxicity of PM in laboratory animals and
13 controlled human exposures. Nearly 600 references were cited
14 in Volume III on health effects. Most notably, there were only thirty-seven (37) references citing studies
15 of associations between daily PM and mortality. Only four of these studies separated PM effects from
16 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/mortality associations not confirmed	3

17
18 The impact of these four association studies cannot be overstated; either in the 1996 PM NAAQS review
19 or in all subsequent reviews including the current ozone NAAQS review.

20
21 Think of it. Four association studies eclipsed the policy relevance of scientific evidence and knowledge
22 presented from hundreds of laboratory and clinical experiments on living organisms documenting
23 anatomical, biophysical, biochemical and systemic homeostatic defense mechanisms common to
24 humans and other mammalian species against natural and ubiquitous atmospheric stressors such as
25 particulates and ozone. The combined weight of physical evidence reported in hundreds more peer
26 reviewed papers published since 1996 (many of which are not cited in the draft O3 PA) provide a
27 substantive scientific bases for ruling out a likely biophysical mechanism for atmospheric ozone induced
28 mortality in mature mammalian organisms.

29
30 COMMENT 5. The EPA should continue to advocate use of association studies in NAAQS reviews; but
31 there are at least two good reasons not to limit itself to the key association study approach. Firstly, it is
32 now conceivable to use heart rate and individual body mass and body surface area, basal metabolism
33 rate and physical exertion levels and local real-time ozone concentrations to calculate personalized
34 respiratory minute volumes and inhaled ozone dose estimates using digital mobile devices. It is now also
35 technically feasible to monitor and collect data from normal and sensitive populations in ad libitum
36 exposure studies involving human volunteers. Such an approach for the collection and analyses of
37 human exposure-response data was not conceivable in 1996. But it is today; and it should be seriously

³ United States Environmental Protection Agency. OAQPS Staff Paper. (1996). *Review of the national ambient air quality standards for particulate matter: Policy assessment of 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

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1 considered by the EPA in future review cycles of ozone and the other criteria pollutants. Secondly, the
2 persistent association study issues of uncertainty and causation can't be resolved by continuing to focus
3 criteria pollutant policy-relevant assessments on key association studies. "A problem can't be solved
4 from the same level of consciousness that created it." (Quote attributed to Albert Einstein.)
5
6

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EXHIBIT A: References on Inflammatory Markers Induced by Exercise and Physical Exertion

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Appendix B

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

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Dr. James Boylan B-2
Dr. Sabine Lange..... B-4
Dr. Corey Masuca B-7

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Dr. James Boylan

Chapter 2 – Air Quality

- Is the discussion on O₃ 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 O₃ 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 O₃ (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?

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- 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?

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Dr. Sabine Lange

Air Quality

- 6) 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 NO_x 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

- 7) 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)?
- 8) 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 3-40⁴ and pg 3-43⁵). 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

- 9) 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

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.”

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1 experience lung function decrements at lower exposures than healthy adults, both models
2 generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations
3 investigated in the controlled human exposure studies.” Is assuming a lack of threshold in an
4 exposure-response relationship a standard method for considering potential at-risk populations
5 that may not have been characterized in an exposure-response assessment?
6

7 10) The EPA also notes in this section that there is a lack of information about the factors that make
8 people more susceptible to ozone-related effects, and that the risk assessment could therefore be
9 underestimating the risk. However, the exposure-response model used to estimate the risk of
10 lung function decrements uses those people in the health population with a greater response to
11 ozone than the mean response (i.e. that fraction of the people in controlled human exposure
12 studies who had FEV1 responses >10%, 15%, or 20%). Does this method already include
13 consideration for more susceptible people in the population?
14
15

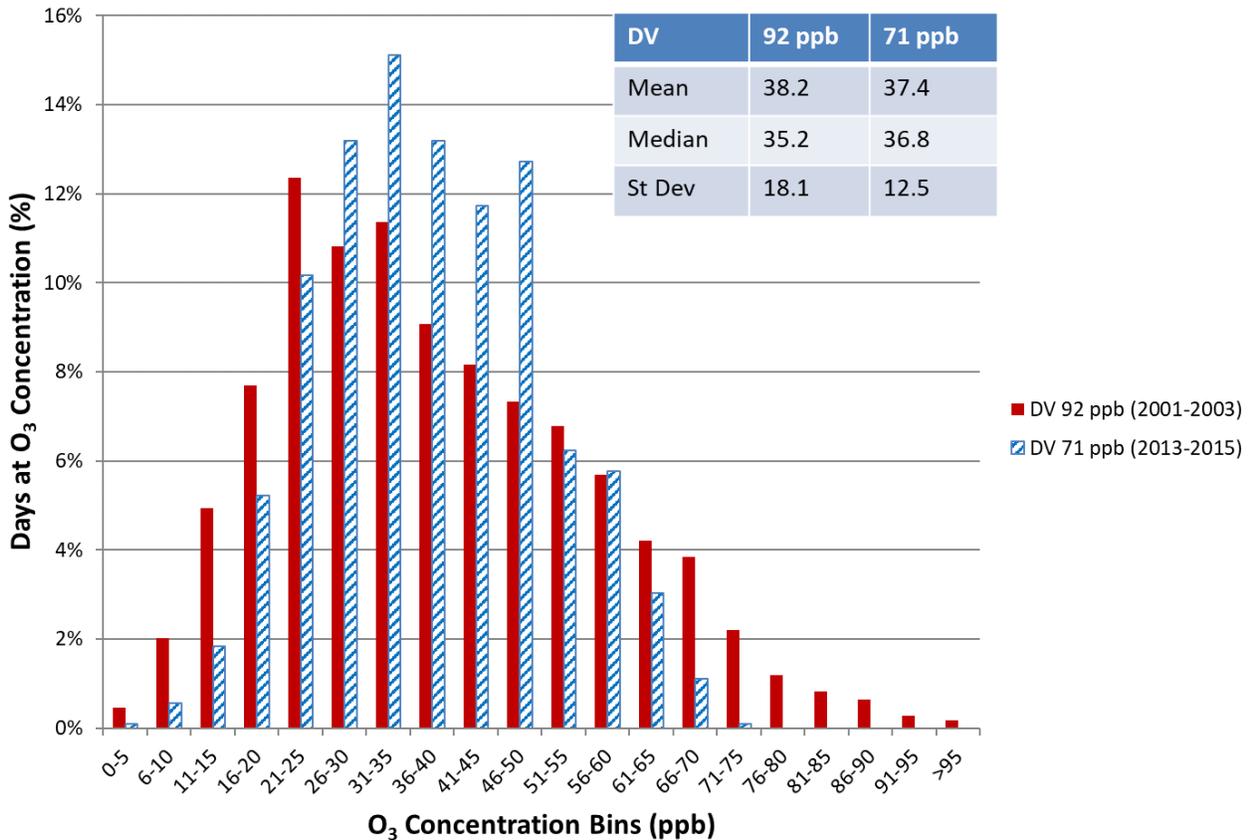
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St. Louis Mean 8-Hr Max O₃ Concentration at Different Design Values



1
 2 **Figure 1.** Distribution of Daily 8-Hr maximum ozone concentrations in St. Louis (averaged over all
 3 monitors in the city) for the 3-year period of 2001-2003 (red bars) or 2013-2015 (hatched blue bars); DV
 4 – design value.
 5
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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?

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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?

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Appendix C

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

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8 **Dr. Dan Jaffe**, University of Washington-Bothell..... C-2
9 **Mr. John J. Jansen**, Southern Company (retired)..... C-5
10 **Dr. Frederick Lipfert**, Independent Consultant..... C-10
11 **Dr. D. Warner North**, NorthWorks C-22
12 **Dr. David Parrish**, Independent Consultant..... C-33
13 **Dr. Sonja Sax**, Ramboll C-50
14 **Dr. Duncan Thomas**, University of Southern California..... C-57
15

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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 NO_x 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 O₃ does not only impact high elevation sites. Its impacts these locations the strongest, but stratospheric O₃ 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 O₃ 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 O₃ concentrations, even in urban areas. Locally generated O₃ will build on these background concentrations. In general, chemical-transport models have made huge progress in their ability to model O₃ due to improvements in grid resolution, chemistry, meteorology, etc. Nonetheless, there are still uncertainties in the magnitude O₃ 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 O₃. (see Figure 2-15). Sections 2.5.1 discuss these natural sources.

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1 Interstate transport of O₃ would not be considered part of the US background so it would not be
2 discussed in this section. That said it should be mentioned somewhere and I do not see it
3 anywhere in the PA document.
4

- 5 6) As with US background, methane contributes to a global scale enhancement of O₃ of around 5
6 ppb. Thus it is a small, but significant contribute to urban O₃ everywhere.
7
8

9 **Response to questions from Dr. James Boylan:**

10
11 I have all of section 2 on air quality. Overall I think it is well down and accurately conveys the major
12 sources of surface O₃ in the U.S. I do have the following comments/suggestions:

13
14 Page 2-3, line 20: add soils.
15

16 Page 2-4, line 9: “volume” ?
17

18 Page 2-7, line 23: Really? I don’t think a lot of companies are making these instruments yet so when and
19 how will SLAMs implement the chemiluminescent monitoring instruments?
20

21 Page 2-18, Figure 2-10: The high elevation site is a bit unusual in showing no diurnal pattern. Typical
22 high elevations sites do show usually show a pattern but can differ from low elevation sites.
23

24 Page 2-21, End of section. As noted by Dr. Lange (see her questions), it is also important to discuss
25 changes at the lower end of the distribution and the annual average O₃ associated with changing NO_x. It
26 suggests that the overall annual average has not changed much, while the high concentrations have
27 declined.
28

29 Page 2-26, line 9: “...global natural AND INTERNATIONAL sources..”
30

31 Page 2-27, lines 25+26: I find this sentence confusing.
32

33 Page 2-28, line 14: Statement about CO is out of context and maybe misleading.
34

35 Page 2-28 line 23: “... are generally small.” ??
36

37 Page 2-29, lines 1-2: I find the discussion on VOCs a bit simplistic. Not everywhere is swamped by
38 biogenic VOCs. See example in Qian et al 2019 (<https://doi.org/10.1021/acs.estlett.9b00160>, 2019)
39

40 Page 2-29, line 7: Order of magnitude is too large. Maybe factor of 2 or 3.

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- 1 Page 2-29, line 20: A new analysis by Buysse (DOI: 10.1021/acs.est.9b05241) strengthens this point.
2
- 3 Page 2-29, line 25: The exceptional event rule should also be mentioned here, as it was for strat-trop
4 exchange.
5
- 6 Page 2-32, line 9-10: I think what's important here is the breakdown between natural and anthropogenic
7 methane. We know the current and historical concentrations fairly well.
8
- 9 Page 2-33, line 13: A good references here is Lin 2015 (DOI: 10.1038/ncomms8105)
10
- 11 Page 2-33, line 21: Really need to define "baseline O₃" here.
12
- 13 Page 2-36, line 11: But a lot of the satellite data is associated with the "apriori" which is another model.
14 Do you distinguish based on the fraction of the apriori in the column?
15
- 16 Page 2-37, lines 1-5: This discussion on model errors and bias really needs at least one figure.
17
- 18 Figures 2-16 and 2-17: I think the captions can be improved here. Might be better to say "Modeled
19 MDA8 from all sources and the components"
20
- 21 Figure 2-20: Is there a difference between MDA8 and 8-hour contributions? Also, clarify this is
22 "modeled MDA8". Can you simplify to "contributions of each sources to the modeled MDA8".
23
- 24 Figure 2-22: Change "Base ppb" to "total modeled MDA8 ppb"
25
- 26 Page 2-50, line 12: "Error"
27
- 28 Figure 2-25: Hard to read this figure. Suggest focusing on period between May-September.
29
- 30 Figure 2-26: Wrong caption. Suggest focusing on period between May-September.
31
- 32 Page 2-59, line 23: Its probably important out that fire emissions and chemistry are a very large
33 uncertainty, larger than the other natural sources. I also suggest to point out the need for better tools to
34 identify these contributions for exceptional event analyses.
35
36

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

2 Given the narrow range of the questions posed by the CASAC members, I read only portions of the
3 draft Ozone Policy Assessment (Chapters 1, 2, 3, Appendix 3C, & portions of Appendix 3D). I have
4 responded to most of the CASAC member questions and also offer some general comments.
5

6 **General Comments**

7
8 For the most part I will not repeat comments made on the draft ISA but many of them apply to this
9 document as well. For example, on page 2-3, implying mobile NO_x is largely responsible for decreasing
10 NO_x emissions ignores substantial reductions in EGU NO_x.
11

12 I continue to be concerned over the lack of a quantitative integrated uncertainty analysis (IUA) both in
13 individual sections as well as overall for the risk numbers presented. Instead, EPA conducts a qualitative
14 analysis by characterizing “the magnitude and direction of the influence on the assessment for each of
15 these identified sources of uncertainty” page 3D-135 (see also pages 3-64 and 3D-87). The document
16 mentions this qualitative approach several times in the document without any “results” being presented
17 nor a reference to where they are (i.e., Table 3D-61 on page 3D-136 (referred to, confusingly, as Table
18 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
19 scenarios are different from each other. I recognize the task is difficult and getting more so as the tools
20 become more complex (e.g., the APEX, HDDM-CAM_x, and Voronoi models). Nevertheless,
21 quantitative uncertainty estimates can be estimated for most if not all steps in Table 3D-61 and IUA
22 methods are available, and have been applied to support comments on past NAAQS reviews. See
23 references provided in ISA comments.
24

25 I agree with the preference for the human exposure studies over the epidemiological studies in terms of
26 having more confidence in their use. This stands in stark contrast to the approach used by EPA in the
27 PM PA. As I stated in my comments on the ISA as it pertains to causality characterization, “quality
28 human and animal experimental studies at relevant exposures need to be weighted over suggestive
29 epidemiological (associational) studies to establish causality.”
30

31
32 **Questions from Dr. Masuca**

33
34 **Questions 1:** The science on stratospheric tropospheric exchange of ozone is well known and discussed
35 briefly in section 2.5.1.1 on page 2-27. While it can lead to a general increase in background ozone, the
36 question is whether and how much it contributes to ozone NAAQS exceedances. The magnitude,
37 frequency, and timing of such events become important. The effect is more pronounced and observable
38 in high elevation western monitors. Much of this is discussed reasonably well in the rest of section 3.5.

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1 Since exceptional events are excluded from the risk analysis, it seems there should be more discussion
2 of the exceptional events policy and the difficulty in making such demonstrations to EPA.

3
4 **Question 2:** All of the networks mentioned, including the road-side monitors provide important data for
5 model performance evaluation and development. The road-side monitors should be mentioned in this
6 regard. I would note that the 3 summer months operating schedule for PAMS sites needs to be re-
7 evaluated. Peak ozone is occurring outside these three months more frequently and data on other seasons
8 is needed.

9
10 **Question 3:** I am assuming you are referring to what is used in the health studies. Although other
11 exposure periods have been used, the human exposure studies summarized in the PA use 6.6 hour
12 exposures. The epidemiological studies have used a variety of averaging time from 1 hour to annual
13 average, including a max daily 8 hour.

14
15 **Question 4:** The diurnal patterns are driven by the relative magnitude of production and loss processes
16 and the relative magnitude is variable across urban, rural, coastal, and elevation locations and time of
17 day. Production is influenced by sunlight, temperature, humidity, etc. Losses include deposition
18 (enhanced under a nocturnal boundary layer) and destruction through fresh NO emissions. While not
19 comprehensive, this section describes the issue adequately.

20
21 **Question 5:** There is always locally generated and transported ozone from various distances. As
22 mentioned above, the issue is how much background ozone contributes to ozone NAAQS exceedances.
23 The magnitude, frequency, and timing of such events become important. The effect is more pronounced
24 and observable in high elevation western monitors.

25
26 US background ozone is a term of art and, as such, is virtually impossible to measure. Even
27 sophisticated monitoring using filtering is problematic from a source oriented point of view (see
28 discussion on page 2-33). Models are uncertain but do track specific sources making them more
29 amenable to a definition of what is included and excluded from US background and can do so for all
30 locations. That said, which method is more accurate is not demonstrated in the document. An
31 uncertainty analysis of the models is possible but explicitly excluded (see page 2-38). I find this
32 paragraph completely inadequate, especially relying of a seasonal mean uncertainty of ± 10 ppb when
33 the risks estimates rely of hourly concentrations at specific locations. Uncertainty estimates need to be
34 estimated in the context of the intended use of data or model results.

35
36 I believe the discussion on international emissions is reasonable and both anthropogenic and natural
37 sources are discussed. All natural sources both foreign and domestic are included in USB. Only foreign
38 anthropogenic are included. All US anthropogenic sources are the other side of the coin and this
39 includes interstate transport (or other US state contributions to a given site).

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1 The discussion of methane is warranted as it contributes to USB. As it is well mixed, its contribution is
2 not very variable in space or time.

3
4
5 **Questions from Dr. Boylan**

6
7 **Section 2.1:** This section seem to be accurate and complete.

8
9 **Section 2.2:** See comments on same subject on ISA.

10
11 **Section 2.3:** See my response to Dr. Masuca's question 2 above.

12
13 **Section 2.4:** See my response to Dr. Masuca's question 4 above.

14
15 **Section 2.5:** See my response to Dr. Masuca's question 5 above. In addition, I continue to be concerned
16 that model performance evaluation is less than robust. See my comments on the PM PA. EPA uses the
17 old justification that performance is in line with the published literature (see page 2-37). The purpose of
18 model performance in the literature tends to be different than the context of regulatory development. I
19 realize this ship has sailed but it is still bothersome. Maybe if we ever get serious in conducting a true
20 IUA, air quality model performance could be conducted in the context of driving the risk assessment.
21 For example, how likely is it that an estimated exposure to one day above the benchmark concentration
22 would actually be exposed to 2 or 4 days, or the reverse, assuming the activity patterns for the
23 population are perfect?

24
25 **Section 3.4.1:** I have several concerns with this section. On page 3-48, the criteria for selecting the 8
26 areas are vague and not quantified. What are "exposure variation" and "population exposure
27 conditions?" How do the eight selected areas vary in these parameters? Both definition and a summary
28 table are needed. There needs to be a concise, simple summary (with examples) on how the ozone
29 concentrations for the micro-environments are derived (page 3-49). I searched and found more detail on
30 page 3D-56. The modeling is quite complex and data intensive. The sheer number of scenarios to be
31 calculated seems quite burdensome and begs the question how accurate these are. What are the
32 uncertainties? Finally, it is not clear how the benchmark concentrations (from the human exposure
33 studies) and dose response relationships (from the epidemiological studies) were derived. This should be
34 included.

35
36 **Section 3.4.2:** Since this is not a national assessment, like the previous section, more information is
37 needed to understand the "diversity" represented by the 8 areas (see page 3-56).

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1 **Section 3.4.3:** The messages in this section is confusing. Contrast the statements on page 3-61 with the
2 summary paragraph on page 3-62. The latter is consistent with the message regarding the just meeting
3 the current standard on page 3-57. EPA should eliminate the modifiers (e.g., markedly) on page 3-61.
4

5 **Section 3.4.4:** See my comments above on the need for a more quantitative integrated uncertainty
6 analysis. The first paragraph describes a qualitative approach but does not direct the reader to where the
7 parameters are summarized. The discussion on page 3-65 implies the adjustments to just meet the
8 various levels is more certain but this is not demonstrated. It needs to be. Similarly on page 3-66 the
9 statement “expected to more realistically estimate activity-specific energy expenditure” needs to be
10 demonstrated. Similarly the last paragraph on page 3-68.
11

12 **Section 3.4.5:** No comments.
13

14 **Section 3C.2:** This section is even more meager than what is in section 3.4.1 (see above) and needs to
15 be expanded to more completely justify the areas chosen and characterize their “exposure variations”
16 and “population exposure conditions.”
17

18 **Section 3C.3:** Page 3C-22 states all monitors were used whether they met data completeness or not. The
19 rationale is based on Appendix U allowing nonattainment designation based on a monitor not meeting
20 data completeness. While I can understand the Appendix U decision, I am not sure it justifies the use of
21 that site for these purposes (i.e., APEX modeling). It would help if the method for filling in missing data
22 were described.
23

24 **Sections 3C.4.1 & 3C.4.2:** On page 3C-23 EPA states “Differences in predicted O3 concentrations
25 between the CAMx-HDDM configuration described here and a standard CAMx v6.5 simulation with
26 full treatment of aerosol-O3 interactions did not influence O3 predictions in the urban study areas
27 examined in this assessment.” This implies that the sensitivities of the version used in the analysis were
28 also not influenced. First, what does not influenced mean? Identical concentrations in every place and
29 hour or something less rigorous? Second, was a comparison made of the sensitivities derived from both
30 models (I recognize the CAMx v6.5 was probably not run in HDDM mode)? If not, I am not sure I
31 would agree with their implication. EPA should demonstrate that the sensitivities were unaffected by the
32 lack of tracking aerosol and cloud processing on the ozone sensitivities.
33

34 EPA did not included agricultural NOx but did include agricultural ammonia (see page C3C-27). For an
35 ozone assessment this seems odd. And yet Table 3C-4 shows an entry for agricultural fire NOx but
36 nothing for agricultural soil NOx. An explanation is needed.
37

38 Again model performance evaluation is not very robust and is much to aggregated. The data used in the
39 risk assessment (the APEX model) is hour and location specific. Only regional/seasonal statistics are
40 presented. How well does thee model do in a specific study area, at individual monitors, across gradients

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1 in a given hour or day? Model performance in the context of its use is needed. How does the
2 performance affect exposure estimates?

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

7
8 **Section 3C.5:** No comments.

9
10 **Section 3C.6:** Why was Voronoi Neighbor Averaging chosen over other methods? A rationale should
11 be given and its uncertainty quantified.

12
13 **Section 3C.7:** No comments.

14
15
16 **Questions from Dr. Lange**

17
18 **Question 1:** While there may be exceptions, I would expect any changes in the annual averages to be
19 small and could go in either direction. One question I would ask is what the epidemiological studies do
20 when the monitors do not operate for the full year, which is the case of most monitors.

21
22 **Question 2:** I am not a statistician but I do not see how it could “protect against” confounding etc.
23 Confounding exists or it doesn’t. If one tests for confounding then maybe the higher statistical power
24 allows it to be demonstrated more reliably.

25
26 **Question 3:** Yes, I believe those statements to be correct. I believe the statements are generally true and
27 the caveat should apply generally, not to just ozone. I suspect the reason it is highlighted here in the
28 ozone proceeding is because ozone concentrations may be more variable than, say, PM among micro-
29 environments. Exposure is very dependent on the integrated levels of ozone in those micro-
30 environments, thus the use of the highly complex and data intensive APEX model. That said, it is not
31 clear that why similar efforts are not done for PM and the other NAAQS. Studies have shown
32 differences in PM and their species between the ambient and homes, restaurants, groceries, etc. In many
33 cases PM is higher indoors due to numerous sources (e.g., cooking, dust, pet dander). Note that indoor
34 sources of ozone (e.g., air purifiers) were explicitly excluded in this assessment. I find it curious that
35 EPA expends so much effort with APEX on ozone and not PM. Finally, the whole APEX discussion
36 implies but does not demonstrate that the complexities added to APEX result in a more accurate
37 exposure estimate.

38
39 **Questions 4 & 5:** I do not have the expertise to address these questions.

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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 O₃ 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 O₃ 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 O₃, 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.

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1 Comments on the bulleted items in PA Section 3.6, "Key Uncertainties"
2

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

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1 9, 10. *Personal exposure by season; activity levels.* Time-activity levels must first be considered in
2 epidemiology before those data could be used in predicting subsequent health effects
3 including benefits from abatement. Clinical ERF data can be used for morbidity such as
4 respiratory effects but not for mortality or hospital admissions.
5

6 Recent epidemiology papers using annual average ozone concentrations.
7

8 Lim CC, Hayes RB, Ahn J et al. Long-Term Exposure to Ozone and Cause-Specific
9 Mortality Risk in the United States. *Am J Respir Crit Care Med.* 2019 200(8):1022-1031.
10

11 Danesh Yazdi M, Wang Y, Di Q et al. Long-term exposure to PM(2.5) and ozone and
12 hospital admissions of Medicare participants in the Southeast USA. *Environ Int.* 2019
13 ep;130:104879.
14

15 Rhee J, Dominici F, Zanobetti A et al. Impact of Long-Term Exposures to Ambient PM(2.5)
16 and Ozone on ARDS Risk for Older Adults in the United States. *Chest.* 2019 Jul;156(1):71-
17 79.
18

19 Hernandez AM, Gimeno Ruiz de Porras D, Marko D, Whitworth KW. The Association
20 Between PM2.5 and Ozone and the Prevalence of Diabetes Mellitus in the United States,
21 2002 to 2008. *J Occup Environ Med.* 2018 Jul;60(7):594-602.
22
23

24 **Questions from Dr. James Boylan**
25

26 **Chapter 2 – Air Quality**
27

- 28 • *Is the discussion on O₃ and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate*
29 *and complete? If not, what additional information needs to be included?*
30

31 Yes, it's adequate for this purpose.
32

- 33 • *Is the discussion on Sources and Emissions of O₃ Precursors (Section 2.2) accurate and*
34 *complete? If not, what additional information needs to be included?*
35

36 Yes.
37

- 38 • *Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3)*
39 *accurate and complete? If not, what additional information needs to be included?*
40

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1 No. Indoor air quality information should be added.
2

- 3 • *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what*
4 *additional information needs to be included?*
5

6 Urban-suburban-rural concentration profiles for various averaging times would be of interest.
7

- 8 • *Is the discussion on Background O₃ (Section 2.5) accurate and complete? If not, what additional*
9 *information needs to be included?*
10

11 It would be useful to have historical trend data on background levels.
12

13 **Chapter 3 – Review of the Primary Standard**
14

- 15 • *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section*
16 *3.4.1) accurate and complete? If not, what additional information needs to be included?*
17

18 I would like to see comparisons of risks by O₃ averaging times (annual, 24-h, 8-h, daily max) by
19 season and health endpoint.
20

- 21 • *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the*
22 *Current Standard (Section 3.4.2) accurate and complete? If not, what additional information*
23 *needs to be included?*
24

25 Indoor infiltration and attenuation should be included.

- 26 • *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality*
27 *Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be*
28 *included?*
29

30 Personal exposures by age group.
31

- 32 • *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what*
33 *additional information needs to be included?*
34

35 No. See the discussion of Section 3.6 above.
36

- 37 • *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not,*
38 *what additional information needs to be included?*
39

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1 This section should include considerations of health risks at background ozone levels for various
2 averaging times.
3

4 **Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses**
5

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

21
22 I have no comments on this Appendix.
23
24

25 **Questions from Dr. Sabine Lange**
26

27 Air Quality
28

- 29 1) *Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have*
30 *demonstrated that in an area where peak daily ozone concentrations have decreased over time,*
31 *over the same period of time the lowest daily ozone concentrations have also decreased (due to*
32 *the NO_x disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are*
33 *your thoughts about the change of annual average ozone concentrations (which tend to be the*
34 *focus of epidemiology studies) with decreases in annual peak ozone concentrations?*
35

36 I used the data for two frequency distributions from Figure 1 to estimate how cumulative
37 risks could depend on the exposure-response function (ERF) threshold. I postulated a linear
38 ERF so that the contribution to the total risk is the product of the frequency and the midpoint
39 of the O₃ concentration bin (Figure 2). With no threshold or up to about 30 ppb, there is no
40 difference in cumulative risk, as is the case with high thresholds (> 80 ppb). In the mid-

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1 range (thresholds from 40-80 ppb), the cumulative risk for the higher design value (DV)
2 distribution is about double that of the lower one while the ratio of the 2 DVs is only 1.3,
3 showing the importance of thresholds. Most epi studies have used some measure of peak O₃
4 rather than the annual average. My own studies (see Appendix) have used the 95th percentile
5 of the daily O₃ averages.
6

7 Epidemiology
8

- 9 2) *Is an epidemiology study with higher statistical power (sample size) innately more protected*
10 *against problems of confounding, error, and bias, than an epidemiology study with lower*
11 *statistical power (sample size)?*
12

13 No; sample size only affects random error. Effects of measurement error, incomplete
14 control of confounders, or a miss-specified model are independent of sample size. Cohort
15 analyses are widely regarded as the best approach to studying long-term effects, but
16 cohort sample size can only be increased by recruiting more subjects or extending follow-
17 up time, which entails aging and loss of the more susceptible subjects.
18

- 19 3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4*
20 *(Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are*
21 *generally assessing the associations between ambient ozone and specific health outcomes and*
22 *are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40*
23 *and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of*
24 *air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to*
25 *ozone, then should this caveat always be considered when evaluating exposure concentrations*
26 *associated with these types of epidemiology studies?*
27

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

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1 Exposure-Response Modeling
2

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

10
11 I’m not aware of any “standard methods” for dealing with thresholds, aside from
12 controlled (clinical) experiments that are sensitive to selection of subjects. A linear
13 relationship may be the default option with noisy data for which the lowest
14 concentrations may be the least reliable. However, there are good reasons to accept the
15 concept of (essentially) zero threshold, that differ between long- and short-term analyses.
16 The time-series model of Murray and colleagues analyzes daily mortality relationships in
17 terms of the combination of subject frailty and air pollution. Death may result from
18 excess frailty or excess pollution or both. As a result, in a sufficiently large population
19 there will likely always be someone sick enough to succumb to a small air pollution
20 perturbation; the threshold depends on the population at risk. The situation with long-
21 term effects is more complicated. They result from cumulative or repeated exposures
22 after a period of latency, so that effects of pollution abatement will be delayed and it
23 becomes difficult to define the appropriate exposure over the periods involved.
24 Background ozone will also play a role. Here the threshold depends on the characteristics
25 of exposure. Finally, health responses during a year will be the result of both long-and
26 short-term exposures, so that even in the absence of long-term effects there may be
27 pollution-related mortality at any outdoor concentration level. Also, different pollutants
28 may be involved at different time scales.
29

- 30 5) *The EPA also notes in this section that there is a lack of information about the factors that make*
31 *people more susceptible to ozone-related effects, and that the risk assessment could therefore be*
32 *underestimating the risk. However, the exposure-response model used to estimate the risk of lung*
33 *function decrements uses those people in the health population with a greater response to ozone*
34 *than the mean response (i.e. that fraction of the people in controlled human exposure studies*
35 *who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration*
36 *for more susceptible people in the population?*
37

38 Most epidemiology studies assume a homogeneous population at risk which may be
39 convenient but is unrealistic. The remaining life expectancies of those aged 65 and over
40 range from one day to 35 y or more with a median around 15 y. (This situation pertains

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1 for populations but not necessarily cohorts, depending on subject selection.) Many air
2 pollution epidemiology studies have shown higher risks for subjects with pre-existing
3 conditions. Lung cancer mortality rates are proportional to the cumulative cigarettes
4 smoked, even though not all smokers get lung cancer. Following this model, we would
5 expect air pollution-related mortality to respond to cumulative exposures from a few days
6 to decades, depending on many other variables including preexisting disease. The answer
7 to this question is thus: Yes, air pollution epidemiology includes all degrees of
8 susceptibility but the most highly susceptible subjects may dominate the group response.
9

10
11 **Questions from Dr. Corey Masuca**

12
13 **1) 2.1. Ozone and Photochemical Oxidants in the Atmosphere**

14
15 *How sound science is this mechanism of ozone transfer between the stratosphere and the*
16 *troposphere?*

17
18 I don't see this as relevant to the setting of NAAQS levels.
19

20 **2) 2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks**

21
22 *While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET,*
23 *National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road*
24 *Monitoring Sites, especially for NO_y?*

25
26 I'm not familiar with these networks.
27

28 **3) 2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards**
29 **Are Met**

30
31 *There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is*
32 *this short-term 8-hour rolling average consistent with short-term actual and scientific studies?*

33
34 I believe so.
35

36 **4) 2.4.3 Diurnal Patterns**

37
38 *While this section refers diurnal patterns of relative ozone concentrations between day and*
39 *night, are these diurnal patterns solely (although mostly are) attributable to temperature? What*

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1 *about stagnant weather conditions? What about the effects on topography/geography in*
2 *determining diurnal patterns?*

3
4 It's my understanding that the mechanism is controlled by UV light and that temperature
5 accelerates the reactions. To sort out these interactions, I would like to see clinical health
6 effect experiments using ozone exposures at various temperature levels. Los Angeles and
7 the Utah Valley offer examples of topographic influences on ozone photochemistry.
8

9 **5) Background Ozone**

10
11 *There, in general appears to be a lot of discussion about background ozone concentrations from*
12 *transport and natural sources. However, are most salient ozone concentrations more localized*
13 *and from anthropogenic sources?*

14
15 This depends on what is meant by "salient" and may depend on contributions of other
16 photochemical oxidants.
17

18 *This section references the utilization of photochemical grid models due to the lack of ability to*
19 *characterize the origins of ozone and the ability to estimate the magnitude of background ozone.*
20 *However, how predictable are these photochemical models, especially given the highly*
21 *photolytic and relative instability of ozone in the atmosphere?*
22

23 This is a question for the modelers. Relevant questions concern indoor, outdoor, and
24 background temporal patterns and diurnal cycles.
25

26 *This section mentions that international emissions sources via transport mostly originate from*
27 *anthropogenic sources. However, is there a possibility that there can be international transports*
28 *from non-anthropogenic/biogenic sources?*
29

30 I suppose so.
31

32 *Also, this section noticeably leaves out non-international, interstate transport of ozone.*
33

34 Interstate transport should be accounted for by the usual photochemical grid models that
35 don't recognize political boundaries.
36
37
38
39
40

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1
2
3
4
5
6
7
8
9

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.

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

2
3 **Daily Mortality Publications**

4
5 Murray CJ, Lipfert FW. Revisiting a Population-Dynamic Model of Air Pollution and Daily Mortality of
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1 **Dr. D. Warner North, NorthWorks**

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

11
12 While the draft PA represents a great deal of work in assembling information, it is disappointing that
13 there is so little new information on human clinical studies or in assessing impacts on asthmatics, as
14 might be measured by hospital admissions or emergency department visits in areas with high ozone
15 levels.

16
17 Although I am not trained as a medical professional I have extensive personal experience with the
18 frequency and severity of asthma episodes. The most common triggers for a bronchospasm (“asthma
19 attack”) come from pet dander, dust mites, and cockroaches, not air pollution.
20 (<https://www.xolair.com/allergic-asthma/what-is-allergic-asthma/allergic-asthma-triggers.html>). These
21 common triggers may be more frequent in low socioeconomic status locations. Asthma patients control
22 their airway reactivity with inhalers such as albuterol, and for more severe cases, corticosteroids. These
23 medications may be needed frequently (several times per week, or even daily). Especially for severe
24 asthmatics, activities involving exercise may be moderately to severely curtailed. Yes, air pollution can
25 trigger or aggravate asthma. (<https://www.asthma.com/what-is-asthma.html>). But the context ought to be
26 considered – for most asthmatics, air pollution at, or near, present standards is a minor contributor to
27 their symptoms and their need for medication. Most asthmatics are not going to do prolonged exercise
28 out of doors, especially on days with an unhealthy air warning. As one who has personal experience
29 over decades with a severely asthmatic patient and also with an adult with cystic fibrosis, I am skeptical
30 about the analysis used in 2014-5 for the previous round of ozone review. The distinction between
31 responses at 60, 70, and 80 ppb exposures is based on only a few studies, most of them not recent.
32 Inflammation is not well defined and measured. Virtually all observed symptoms including lung
33 function decrements (FEV1) and airway reactivity are transient, going away after a few hours to a day.
34 But: exposure to unhealthy air in the form of a wildfire smoke plume persisting over a metropolitan area
35 for many days should be viewed as a serious public health threat to people such as the two I am close to.
36 Exposure or potential exposure to smoke plumes this year and last year have motivated decisions about
37 getting masks, special filters for air conditioning systems, and sending the sensitive person(s) out of the
38 affected area until the air clears.

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1 Nearly four decades ago, at a time when I was first involved in working on air pollution health effects,
2 there were repeated episodes in a European city of asthma attacks in which many people went to
3 hospital emergency departments for treatment. The incident was initially blamed on air pollution from
4 an electric power plant. More careful investigation indicated it came from unloading ships in the harbor,
5 and the main culprit was soybean dust. The reference is Antó et al., *New England Journal of Medicine*,
6 1989. Yes, air pollution can trigger episodes of asthma attacks across an urban area. But indoor air
7 pollution from pets, dust mites, and cockroaches is much more likely to be the trigger for asthma attacks
8 in urban areas of the United States.
9

10 The studies listed in Appendix 3B on emergency department visits (EDV) and hospital admissions for
11 asthma include numerous ones on New York City and Atlanta, Georgia. I found only one, state-wide
12 study for California, Malig et al., 2016, with data from 2005-2008. This study showed a small increase
13 (1.5 to 3.9% per 10 ppb O₃) for EDV for asthma and upper respiratory infections using warm season
14 data. (Full year results were slightly smaller.) A little less than half of the EDVs were for children 18
15 and under, rather than adults. I would characterize these results as weak association evidence motivating
16 further studies. The authors' final sentence is, "Studies examining the health benefits of ozone
17 reductions should try to account for ozone-EDV relationships to get a fuller picture of those benefits." I
18 heartily concur.
19
20

21 **Questions from Dr. Corey Masuca**
22

23 1. I do not have a background in the specifics, but I believe the mechanism has been well
24 established in the scientific literature for many decades. Here is a reference to an article by a Norwegian
25 scientist from 1960: [Storebø, Per B., "The exchange of air between stratosphere and troposphere,"](#)
26 [Journal of Meteorology 17:547-554 \(1960\).](#) During the 1960s there was much interest in the radioactive
27 isotopes from nuclear testing coming from the stratosphere into the troposphere. There are many other
28 papers you could find with a search on the web.
29

30 2. Near Road Monitoring sites are most important for determining how ozone and precursors
31 change between emissions on a road or highway and ozone levels at locations a short distance away. The
32 ambient air monitoring discussed in this section and Section 3 is at the regional and national scale, rather
33 than the local scale. I note for your attention my responses to Dr. James Boylan regarding Section 3 and
34 Appendix 3C. The calculations made by EPA for its Section 3 analysis were done with a national model,
35 CAMx, with a 12 km by 12 km grid. That is the size of the City of San Francisco, 50 square miles!
36 Local peaks and valleys in ozone levels are not predicted with a model of this large grid size. There are
37 comparisons in 3C.4.2 of model predictions at the grid cell level and monitoring station(s) within the
38 grid cells. The figures in this subsection show the relatively large differences between the model
39 predictions and MDA8 observations. Only one year of data is used for the model predictions. I believe
40 use of a model with a much finer grid size would be useful for areas violating the present standard, and

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1 data from *all* the available monitoring stations should be collected and used. It would be important to
2 examine multiple episodes over many years of prolonged high ozone levels, not just one year, to
3 determine the mix of ozone created out of the local area with ozone from local and nearby NO_x and
4 VOC sources. I did not find evidence in Section 3 and Appendix C that EPA has done such local
5 analysis or emphasized prolonged high ozone episodes from multiple years. Section 3C.6 describes a
6 mathematical system (“Voronoi Neighbor Averaging”) for scaling the CAMx predictions at the
7 monitoring sites to census tract centroids, and these interpolated predictions of ambient ozone levels are
8 used to predict the incidence of health effects for the people in the census tract. (See page 3C-91 for an
9 illustrative diagram. See Figures 3D-2 to 3D-5 for pictures of the census tracts.) Local chemistry of
10 ozone formation and absorption on a scale of less than about 10 miles cannot be done with this EPA
11 modeling system. Ozone peaks produced by, for example, rush hour traffic concentrations in an urban
12 area cannot be examined: the “grain size” of EPA’s analysis is too big! Compare to the data in Figure 2-
13 5, page 2-12. In the 2015-2017 data the exceedances of the MDA8 70 ppb are appearing only in one
14 broad region, California’s Central Valley plus Los Angeles to San Diego (coastal urban areas with
15 mountains to the east creating a “mountain bowl”; the Central Valley is a big “mountain bowl”) -- and in
16 a small number of urban areas – Phoenix, Seattle, Salt Lake City, Denver, Dallas, Houston, Chicago,
17 and the Boston- Washington corridor. It would be useful to have analysis that focuses on these (non-
18 California) urban areas in finer detail. My concern for the California region is that wildfires may play a
19 critical role in causing a large fraction of the red and orange circles in Figure 2-5, which are exceedances
20 of the current 4th worst 8-hour-average day-in-a-three-year-period (MDA8) standard. We should know
21 more about the exceedances in the urban areas other than in California, which are not due to wildfires
22 but to other sources of NO_x and VOCs.

23
24 3. I am not expert on the details, but I think there is a well-defined protocol for computing the
25 maximum 8-hour average from hourly concentrations. I believe it is described in one of the Appendices,
26 probably in the ISA if not the PA, but in my available time I did not find a page reference to give you.
27

28 4. Sunlight drives the photochemical formation and destruction processes for ozone, so what is
29 being discussed in section 2.4.3 is primarily related to the presence/absence of sunlight, that is, day
30 versus night. The length of the day enters as seasonal variation. Temperature and
31 topography/geographical factors affecting air movement are all important for understanding the
32 processes for formation and destruction of ozone. This complexity should be included in the modeling.
33 As I have described under 2, EPA’s system cannot accommodate local detail.
34

35 5. My big concern on 2.5.1.3, including wildfires as part of Background, “USB.” I think wildfires
36 as well as prescribed fires should be considered as anthropogenic sources and not as background.
37 Wildland fires can lead to levels of both PM_{2.5} and ozone far above current standards. At least in this PA
38 “wildland fires” get called out for a heading in the *Table of Contents* and two paragraphs that make it
39 clear that wildfires fires can be an important contributor to ozone exposure in regions where these fires
40 occur. The high exposures from large wildfires should not be kept out of sight by deleting them from the

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1 data as “exceptional exceedance” events. They should be considered as the consequence of human
2 activity – in particular, national, state, and local policies that influence the occurrence and severity of
3 wildfires. The adverse health effects are quite real to those who suffer them. Whether or not a state gets
4 relief from whether these “exceptional exceedances” trigger a finding of non-compliance with a
5 NAAQS may be important because of penalties for non-compliance. That is a separate matter from
6 protecting public health.

7
8 6. Methane can be the VOC that forms ozone in the presence of NO_x and sunlight. Usually other
9 VOCs are more important, but if these others are not present then methane contributes to NO_x
10 formation. The ISA had extensive discussion on the role of methane. Yes, it is true that in our post-
11 industrial society we have a lot of sources of methane such that there is much more than in pre-industrial
12 times, and we are uncertain on how much more methane we now have. But that uncertainty will be
13 much more important for climate alteration from CH₄ as a greenhouse gas than for methane contributing
14 to peak levels of ozone above the primary standard. I would say that extensive discussion should be in
15 the ISA rather than the Policy Assessment, since controlling sources of methane is not a focus for the
16 Policy Assessment document now under review. I do not find the three-paragraph discussion in 2.5.1.6
17 as inappropriate as I do the huge amount of complex detail elsewhere in this long document.
18
19

20 **Questions from Dr. James Boylan**

21
22 Overall, for the three portions of the PA that you chose to ask about, your question of whether it is
23 accurate and complete has led me to comment on what I think about the whole PA draft document,
24 which I have done in my earlier general comments. By and large, I think EPA staff have worked hard
25 and done a good job in assembling a great deal of relevant material. I don't think any document of this
26 type can ever be judged as complete. I think a major goal of the document should be to focus attention
27 on research needs as well as policy needs. The document should be an evolving guide to both
28 government officials and interested parties on the public. Trying to make it more “complete” might add
29 much more detail that is superfluous to the interests of most readers. It should be accurate in the sense
30 that it does not mislead readers. The material on inflammation at low exposure levels in the ISA draft is,
31 in my judgment, at least borderline misleading in suggesting evidence for inflammation at levels at or
32 below the standard. As I expressed in my ISA comments, I thought the support for these statements in
33 the ISA was weak. The discussion in the PA seems a bit better in citing what was actually written by
34 authors of the studies. Section 3.5, page 3-74 line 29-232 cites the ISA rather than the preceding portions
35 of the PA. I repeat my objection to the words, “respiratory inflammation” in this sentence as inaccurate
36 as stated, without any caveats. Two sentences on page 3-76, lines 9-14, are slightly better, indicating that
37 “inflammatory response and airway responsiveness” are “reported for higher exposure concentrations”
38 rather than at “concentrations slightly above 70 ppb with intermittent exercise.” See also footnote 69,
39 page 3-76.
40

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

7
8 Chapter 3: Review of the Primary Standard. You focus your questions not on this whole chapter, but on
9 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
10 available evidence as of 2019 and the recommendation that the primary standard, lowered in 2015 from
11 MDA8 75 ppb to 70 ppb, be maintained, or the discussion of the Administrator’s reasoning in revising
12 the standard from MDA8 75 ppb to 70 ppb, described in Section 3.1.1.

13
14 There is relatively little that is new in the 28 pages. Almost all of it is very similar to what was provided
15 in the EPA Health Risk and Exposure Assessment (HREA) in 2014. Is the reasoning used by the
16 Administrator (after advice from CASAC and the public) valid today? Is there important new
17 information? Might the standard be viewed as overprotective, compared to the previous standard of 75
18 ppb? Or is it in need of further tightening? Children including asthmatic ones in the Sacramento area
19 experience MDA8 exposure well over the 75 ppb level. How much of public health problem does this
20 pose? Asthmatics and children in other urban areas are experiencing levels in the high 60 ppb range and
21 above. Is their health being protected with an adequate margin of safety? What strikes me as odd is that
22 there is so little described in Section 3.5 beyond the reasoning of a previous Administrator described in
23 Section 3.1.

24
25 You asked about Appendix 3C, which presents a great deal of information on population exposure.
26 Appendices 3C and 3D support the Section 3.4 modeling exercise on how many health effects might be
27 expected with reductions in ozone precursors such that the eight metropolitan areas just meet a MDA8
28 standard, with calculations for 75, 70, and 65 ppb. The Appendix 3C material is extremely detailed, and
29 it does not tell us about the extent of observed or predicted public health effects under current levels of
30 ozone exposure, as opposed to these projected “design values” to just meet a standard.

31
32 Here are some brief notes on Sections 3C.2 to 3C.7. In Section 3C.2 EPA describes the eight study
33 areas. The section does not explain in any detail why these eight were selected – seven are holdovers
34 from 2015. The extent of the explanation is one sentence, lines 8 to 10 on page 3C-13. Section 3C.3,
35 Ambient Air Ozone Monitoring Data, describes the procedure for determining the NOx emissions
36 changes needed to meet the three MDA8 standards. The maps show us the location of monitors,
37 including buffer sites used for interpolation for modeling air quality. Section 3C.4.1 tells readers that the
38 CAMx model was used with the Higher Order Direct Decoupled Method (HDDM). The CAMx model
39 covers the lower 48 states and adjacent areas of Canada and Mexico with a 12 by 12 kilometer grid, and
40 it was run for all of 2016 including a startup period in late 2015. (This is one year of weather, with a grid

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1 cell size of 50 square miles. Local scale phenomena will not be captured in such a system.) Weather data
2 for 2016 came from a mesoscale numerical weather prediction model, and 36 vertical layers are used for
3 this and for CAMx. (Later in the 3C text 44 levels are indicated.) The alpha version of the Inventory
4 Collaborative 2016 emissions was used. Emissions for wildfires and prescribed burns were included. (If
5 any periods were deleted as exceptions, this is not noted, and **any such exclusions of emissions should**
6 **be disclosed**.) 3C.4.1.6 describes initial and lateral boundary conditions. Section 3C.4.2 discusses how
7 well the CAMx model can reproduce the actual measured 2016 O₃ concentrations. We are told the
8 predictions “generally reproduce patterns of observed O₃. The notable exception is a persistent
9 underestimate in winter across almost all regions, particularly at the higher latitude sites.” (page 3C-29,
10 lines 2-4.) Then a large amount of statistical data and maps are given in support.

11
12 EPA has amassed a huge amount of detail on modeling ozone in ambient air nationally on a large grid.
13 Details about local topography and sources such as concentrations of vehicular traffic and major
14 stationary sources are absent. There is no calculation at this stage on what is in indoor air, as opposed to
15 outdoor air. Does the smoke plume from a large nearby wildfire blow into a metropolitan area, or does
16 the plume bypass the area? This depends on the wind direction. Data from only one year will not reveal
17 patterns that may cause the peak ozone exposures over a period of three years, five years, or longer. For
18 seasonal ozone averages over the lower 48 states I would expect a general match, but I doubt if peak
19 ozone concentrations leading to MDA8 standard exceedances at individual monitors will be well
20 reproduced. Figure 3C-13 to 16 indicate a normalized mean bias of the order of 20 ppb in the
21 northeastern United States, with a larger discrepancy in winter. For concern about peak ozone levels in
22 the Washington to Boston metropolitan corridor, that is not great accuracy. In the west with higher
23 background, the validity of the model prediction may be even more questionable in terms of the
24 frequency of exceedances above the standard at specific monitors. See Figures 3C-40 to 43.

25
26 Section 3C.5 discusses air quality adjustments, specifically, reductions in NO_x emissions to just meet
27 the standards. We are told that EPA used this approach for the 2015 O₃ NAAQS review. This is an effort
28 (using a very detailed model of only moderate accuracy on a regional basis) to predict ozone levels if
29 NO_x reductions were made so as to allow the standards to be just met. The chemistry is non-linear, and
30 so there is an HDDM adjustment process. In some metropolitan areas (e.g., Sacramento) big emissions
31 reductions will be needed to meet standards.) Then in 3C.6 we learn about interpolating from a 12
32 kilometer grid size to 500 meters and centroids of census tracts. How well does this work in downtown
33 urban areas with street canyons? What is the variability of ozone readings within a few kilometers of a
34 monitor?

35
36 In 3C.7 all of this is put together to compute results, design values for patterns of ozone exposure over
37 the urban areas. Perhaps something can be learned from this exercise, but it should be realized that it is
38 an effort to go from a lower 48 scale to predict on a “neighborhood” scale, with assumptions
39 compounded all along the way.

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

9 The collection of models and assumptions produces apparently precise numbers about how many health
10 effects might occur under alternative standards. See the discussions supporting the choice of a 70 ppb
11 standard in Section 3.1 and 3.5. The key uncertainties not covered in 3C are the assumptions about
12 human behavior, exercise patterns, and exposures outdoors and indoors where the presence or absence
13 of air conditioning may be important. (The methods are described in Appendix 3D.) I would like to see
14 regional studies using local models, knowledge about socioeconomic status by neighborhoods and
15 involvement of state and local air pollution experts who might know about “hot spots” of peak exposure,
16 and their proximity to schools, playgrounds, sports arenas, and other locations where children and adults
17 might be exercising out of doors for the order of six to eight hours. And do the exposed people learn
18 about unhealthy air conditions and change their behavior so as to avoid exercising at times of high
19 ambient ozone levels? In the unhealthy air from recent wildfires in northern California, schools were
20 closed and sporting events were cancelled. Does an asthmatic want to ride her bike to work on a
21 unhealthy air day, or will she opt for using her car or public transportation?
22

23 Section 3.6 of the PA describes key uncertainties and areas for future research. There should be much
24 more attention to “understanding of O3 effects” in the range of 70-120 ppb, and not at “below the lowest
25 concentrations studied,” which would mean below 60 ppb (page 3-88). Human behavior is hard to
26 predict. Better understanding is needed on who is at high risk by exercising outdoors under high ambient
27 ozone conditions. Sensitive subgroups such as children and asthmatics need to be protected. How great
28 is the need for protecting them in areas and cities experiencing MDA8 exposures near and above 70 ppb,
29 sometimes above 100 ppb, based on Figure 2-5, page 2-12?
30

31 What EPA staff did in examining eight metropolitan areas was to model ozone exposures under a set of
32 assumptions that emissions reductions would occur such that these areas **would just comply** with the
33 standards. Were the health impacts predicted at these computed-by-model with assumed patterns of
34 human activity judged to be acceptable for protecting public health with an adequate margin of safety?
35 Yes. that was the claimed goal for the analysis, to enable an evaluation of model predictions of health
36 effects from model predictions of air quality. There is little evidence that EPA worked with its Regional
37 Offices, with state agencies, and the research community **to ascertain the magnitude of the public**
38 **health impacts of recorded actual ozone exposures** in the most recent years, from 2015-2017 to the
39 present, in areas where exposures exceed the standards by a large amount. Why not, as a supplement or
40 a better use of EPA resources, go to Sacramento as the city with the highest ozone exposure (e.g., Figure

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1 3C-81, page 3C-114; Figure 3C-103, page 3C-138) and learn more from the medical professionals in
2 this metropolitan area about the extent to which asthmatic children in that area were suffering health
3 exacerbation, such as inflammation, pain on inspiration, and increased airway responsiveness?
4 The numbers in Table 3.3 page 3-58 reflect that with air quality just meeting an MDA8 standard of 70
5 ppb, exposures at 80 ppb and even 70 ppb are quite rare, and exposures above 60 are relatively
6 infrequent, an average of 3 to 9% for children with asthma and slightly less of all children experiencing
7 one day per year of exposure while breathing “at an elevated rate.” Compare Table 3-5, with air quality
8 just meeting a higher MDA8 standard of 75 ppb. The numbers for affected children nearly double to
9 about 7 to 16%, because exposures above 60 ppb are projected to increase by that much.

10
11 Sacramento is far from meeting a 75 ppb standard. In order *to bring Sacramento into compliance with*
12 *the present MDA8 70 ppb, a reduction of 58% in NOx precursor emissions is estimated to be needed.*
13 A 45% reduction would be needed to meet the old standard of 75 ppb. These are a big numbers! No
14 others of the seven metropolitan areas would need more than a 23% reduction in emissions to meet the
15 old standard of 75 ppb. IF the standard were reduced to 65 ppb, Sacramento would need a reduction of
16 72% and the need for the other seven areas would be in the range from 38 to 68%. The numbers are
17 large for Sacramento because Sacramento has a high background ozone level, “USB,” as EPA uses this
18 term. Phoenix also has high background. Phoenix could meet the 75 ppb standard with an emissions
19 reduction of 14%. But for the 70 ppb standard, Phoenix would need to reduce its emissions by 49%,
20 approaching the high number for Sacramento. Some of that ozone comes from wildfires, now counted as
21 background. Note in Figure 3C-103 the red squares in the observed data, above and below Sacramento
22 in rural adjacent counties. These might have come from the large wildfire plume(s) in the year 2017.
23 (Numbers in this paragraph come from Table 3C-19, page 3C-89.)

24
25 **Critical commentaries on EPA’s modeling.** The PA and the ISA do not acknowledge published
26 criticisms of the methodology used in 2014-15, and used again in this 2019 PA with only minor
27 changes. I have not have the time to find more than a few examples of such criticism, but in reviewing
28 three EPA draft documents I have found little evidence that EPA has included criticisms in peer-
29 reviewed journals, presentations at EPA public meetings, and written comments from members of the
30 public.

31
32 In my comments on the Ozone ISA I discussed the Belzer–Lewis paper recently published (2019) in
33 *Risk Analysis*. I will not repeat these comments, which CASAC members should have in my earlier
34 submission on the ISA. Another paper pointing out the uncertainty in estimating FEV1 decrements is
35 Glasgow and Smith (2017). Modeling uncertainty on the concentration response relationship should be
36 considered as well as statistical uncertainty. Neither of these papers is referenced or discussed in the ISA
37 or PA. The Glasgow-Smith paper discusses the methodology used in EPA’s Health Risk and Exposure
38 Assessment (HREA) from 2014. Essentially the same methods appear to have been used in generating
39 Table 3.3, based on the McConnell et al. papers from *Inhalation Toxicology*, 2012 and 2013. (See
40 footnote 64, page 3-57, which explains that there are “a number of differences between the 2014 HREA

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1 and the quantitative modeling and analysis” in the PA, with these details discussed in Appendix 3D. The
2 HREA and the two McDonnell et al. papers are referenced in the PA Section 3.

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

14
15
16 **Questions from Dr. Sabine Lange**

- 17
18 1. I fully agree that the decrease in annual average ozone exposure is significant. I continue to have
19 concerns on whether the epidemiological results imply manipulative causality as opposed to
20 association, and I am pleased to read that EPA is not using these epidemiological results but
21 rather basing its recommendations (for the last round and the present one) mainly on human
22 clinical studies. There are still areas of the US, such as the Sacramento area, that have MDA8
23 levels well above the current standard of 70 ppb. I would like to see CASAC focus on the public
24 health risk in these areas. See my general comments above regarding asthma. There ought to be
25 more research to see if high ozone episodes in Sacramento (and elsewhere in the Central Valley
26 and the Los Angeles to San Diego area) have led to increases in hospital admissions and
27 emergency department visits.
- 28 2. No. I responded to a similar question in the O₃ ISA. Statistical power comes from having a large
29 sample size, and NOT from having resolved issues of confounding, error, and bias. Consider we
30 have a study of 10 million children showing that shoe size predicts reading ability. Because data
31 were obtained from 10 million children, a very large number, the confidence interval is quite
32 narrow. Does this apparently accurate prediction imply that getting children larger shoes will
33 improve their reading ability? No way!
- 34 3. I am inclined to think that the problem is a general one that will only be resolved by getting data
35 on potential confounders such as income (more generally, socioeconomic status), and extremes
36 of temperature, which have large impacts on mortality and morbidity via mechanisms
37 independent of air pollutants. However, we should understand that at VERY high exposure
38 levels, air pollutants such as ozone and fine particulate matter (e.g., smoke) can cause illness and
39 death. The shape of the exposure-response relationship is critical for assessing the risks.
40 Extrapolation over orders of magnitude is readily done with available mathematics. But how this

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1 extrapolation is done should reflect judgment on the biological mechanisms underlying damage
2 to health.

- 3 4. Yes, assuming a lack of threshold has become a standard method in many areas of EPA’s risk
4 assessment practice. Many of us old-timers believe this practice is questionable, because absence
5 of evidence is not evidence of absence. The biological mechanisms underlying the adverse health
6 response should be assessed based on available information including judgment. Traditional
7 toxicology has used a sigmoid shaped exposure-response function, on the basis that very small
8 exposures (episodic or cumulative) are unlikely to trigger an adverse response but as the
9 exposure increases, the body’s defenses and repair mechanisms can become inadequate, so the
10 adverse effect becomes common in an exposed population. And the response may saturate with
11 most or all of those who are susceptible to it having the adverse response – e.g., given enough
12 bacteria in the spoiled food, nearly everyone gets sick from eating it. But linearity to zero
13 became common in cancer risk assessment. This assumption was originated as a health-
14 protective default assumption for screening: a plausible upper bound for identifying chemicals
15 deserving more detailed risk analysis, and not for estimating the incidence of human cancer. But
16 linear to zero is often used for the latter purpose.
- 17 5. I am concerned that FEV1 decrements are not a good indicator for adverse health impacts in
18 sensitive populations. (See my general comments at the beginning of this response. FEV1
19 measurements vary a good deal. The Belzer-Lewis paper mentioned in my O3 ISA response has
20 perceptive criticism about using FEV1 data in research.) It seems to me that lack of information,
21 referring to the words you use in your first sentence, (1) should motivate detailed studies of the
22 people that are judged to be at highest risk, and (2) leaders of agencies such as EPA should think
23 beyond legally required standard setting to the bigger issue of how to protect public health with
24 an adequate margin of safety. If adverse health effects are judged to be essentially absent for
25 much of the United States (a reasonable inference from Figure ES-1 in the ISA and Figure 2-5,
26 page 2-12 in the PA), then attention should be focused on the remaining areas where such
27 adverse health effects may still be occurring. Are these adverse health impacts really there in
28 these remaining areas, or are our government officials being overly precautionary and protective
29 in setting standards, but ignoring major public health protection needs by assuming that some
30 causes, such as wildfires, are “natural background?” ***EPA should be using common sense and
31 not be trapped in traditions that violate common sense.*** The levels of ozone and fine particulate
32 matters that millions of people in California have experienced from wildfire smoke plumes in
33 2017, 2018, and 2019 are far above the NAAQS standards and pose serious health effects,
34 especially to members of sensitive subgroups. Some of these people are among my family, my
35 friends, and my neighbors. The costs involved in reducing these risks to health from wildfire
36 plumes are very large. So are the costs of bringing ozone levels in Sacramento into compliance
37 with a 70 ppb MDA8 standard, even if with wildfire periods are exempted. (In my humble
38 judgment, the former activity makes much more sense than the latter.) EPA staff and CASAC
39 should acknowledge these facts in their written documents, as part of advising the EPA

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1 Administrator on strategy with respect to criteria air pollutants. I believe giving such advice is
2 within the legal mandate of CASAC under the Clean Air Act.

3
4 Comment: I appreciate and endorse the message in the graph you show in your questions for the
5 St. Louis area comparing 2001 to 2003 with 2013 to 2015. Please consider also a graph of the
6 same sort of data for the Sacramento area for 2017-2019, compared to earlier years with no big
7 wildfires, such as 2013 to 2015. The message will be almost opposite. Compliance is not nearly
8 achieved, but a distant and receding goal, especially if wildfires are not exempted.
9

10
11 **References not in the PA**

12
13 Garrett Glasgow and Anne E. Smith, “Uncertainty in the Estimated Risk of Lung Function Decrements
14 Due to Ozone Exposure,” *Journal of Exposure Science and Environmental Epidemiology* 27:535-538,
15 2017.

16
17 Alexandra E. Larsen, Brian J. Reich, Mark Ruminiski, Ana G. Rappold, “Impacts of fire smoke plumes
18 on regional air quality, 2006–2013.” *Journal of Exposure Science & Environmental Epidemiology*,
19 2017; DOI: [10.1038/s41370-017-0013-x](https://doi.org/10.1038/s41370-017-0013-x). Summary in *Science Daily*:
20 <https://www.sciencedaily.com/releases/2018/01/180109112415.htm>.

21
22 J.M. Antó, J. Sunyer, R. Rodriguez-Roisin, M. Suarez-Cervera, and L. Vazquez, “Community outbreaks
23 of asthma associated with inhalation of soybean dust,” *New England Journal of Medicine*,
24 320(17):1097-1102, 1989.

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1 **Dr. David Parrish, Independent Consultant**

2 **Questions from Dr. James Boylan**

3
4 **Chapter 2 – Air Quality**

- 5
6
 - *Is the discussion on O₃ and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate and complete? If not, what additional information needs to be included?*

7
8
9 The last sentence of the first paragraph of Chapter 2 lists 4 important factors that affect concentration of
10 ozone and other photochemical products. Deposition to surfaces should be added as a 5th factor, as it has
11 a strong effect on ambient ozone concentrations.

12
13 The sentence on lines 31-33 of page 2-2 is not correct. It would be accurate if revised to read: “This
14 mechanism is similar to the chemistry driving summertime O₃ formation, although the photolysis of
15 VOCs is a more important primary radical source in winter. In summer, the major primary radical source
16 is the photolysis of O₃ to form an excited state O atom, which then can react with water to form OH
17 radicals.”

- 18
19
 - *Is the discussion on Sources and Emissions of O₃ Precursors (Section 2.2) accurate and complete? If not, what additional information needs to be included?*

20
21
22 As I have stated in previous responses, the uncertainty of the ozone precursor emissions estimates
23 should be clearly discussed and defined to the extent possible. This section gives no indication of the
24 precision and accuracy of the estimates, except the total emissions of the precursor classes are given to 5
25 significant figures, which is misleading. I think that a paragraph should be included that discusses
26 emission inventory uncertainty. One example of inventory uncertainty is the differences in emissions
27 between those discussed in Section 2.2 and those actually used in the photochemical modeling discussed
28 in Appendix 3C. (This comment largely repeats a comment that I made in my response to a similar
29 question regarding the PM PA; more details are given there.)

- 30
31
 - *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?*

32
33
34 I find the discussion in this section to be accurate and complete.

- 35
36
 - *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what additional information needs to be included?*

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1 The discussion in this section is reasonably accurate and complete, but there are some subtleties that
2 should be discussed to more clearly inform the reader. In Figure 2-5 relatively large symbols are used
3 for each monitor color coded to indicate the 2015-2017 design values. The points with the largest design
4 values are plotted last, so in urban areas with many monitors, one can only see the monitors with the
5 largest design values. As a consequence, the plot gives a somewhat biased picture. If this figure used
6 smaller symbols, the bias would at least be partially corrected. Figure 2.6 has a similar bias with larger
7 symbols plotted last indicating the largest decreases, and smaller decreases and increases plotted first
8 and with smaller symbols.
9

10 The conclusions drawn from Figures 2-7 and 2-8 do not adequately reflect the tremendous success of the
11 U.S. effort to reduce ambient ozone concentrations. Figure 2-7 does accurately show that there has been
12 a 32% decrease in U.S. annual 4th highest MDA8 levels since 1980, but that 32% does not consider the
13 U.S. background ozone concentration that emission controls cannot directly affect. Parrish et al. (2017)
14 and Parrish and Ennis (2019) show that when the percent decrease is based on the enhancement of those
15 levels above what would be present from U.S. background ozone alone, then the percent decrease since
16 1980 is >80% (i.e., a decrease of more than a factor of 5). As the discussion notes, “the trend in the
17 annual 4th highest MDA8 concentrations has been relatively flat since 2013, and the design values have
18 been relatively constant since 2015.” The primary reason for this behavior is that there is not much room
19 left for improvement: < 20% of the 1980 enhancement above background. In my view this issue should
20 be emphasized in the discussion of Figures 2.7 and 2.8 as well as in a similar plot in Figure 2-14.
21

22 The discussion of Figure 2-9 emphasizes that the five eastern U.S. regions have all shown decreases of
23 at least 10 ppb in median annual 4th highest MDA8 values since the early 2000’s, while the four western
24 U.S. regions have all shown decreases of less than 10 ppb. It should be emphasized that this is primarily
25 due to the eastern regions having, on average, more anthropogenic ozone in the early 2000s, which
26 could be reduced., than in the western U.S. The reason this is not so obvious from figure 2-9 is that the
27 U.S. background ozone is higher in the west. If that figure showed the enhancement of the 4th highest
28 MDA8 values above the 4th highest MDA8 values that would be present from U.S. background ozone
29 alone, then this point would be more obvious.
30

31 In Figures 2-10 and 2-11, the meaning of the boxes, lines and points should be explicitly stated as done
32 in Figure 2-12.
33

34 The paragraph on lines 11-17 of page 2-19 reads: “Panel B shows the seasonal pattern for an urban site
35 in Baton Rouge, LA. Throughout the southeastern U.S., the highest O₃ concentrations are often observed
36 in April and May due to the onset of warm temperatures combined with abundant emissions of biogenic
37 VOCs at the start of the growing season. This is often followed by lower concentrations during the
38 summer months, which is associated with high humidity levels that tend to suppress O₃ formation. Some
39 areas, particularly in the states bordering the Gulf of Mexico, may experience a second peak in O₃
40 concentrations in September and October.” My understanding of the double peak behavior of ozone

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1 along the Gulf coast is that a particular meteorological pattern (i.e., the development of the Bermuda
2 High) brings cleaner Gulf of Mexico air into the region during the mid-summer months, and more
3 polluted continental air into the region before and after those months. I am not aware of any mechanism
4 by which high humidity levels tends to suppress O₃ formation.

- 5
- 6 • *Is the discussion on Background O₃ (Section 2.5) accurate and complete? If not, what additional*
7 *information needs to be included?*
- 8

9 (Note: some of the material here is similar to my responses to questions regarding background ozone in
10 the O₃ ISA.)

11

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

19

20 Footnote 17 is incorrect. Ozone concentrations that do not include contributions from U.S.
21 anthropogenic emissions can indeed be determined exclusively from O₃ measurements (see Parrish et
22 al., 2017; Parrish and Ennis, 2019), although it is true that they cannot be directly measured.

23

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

33

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

39

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1 Section 2.5.1.6 on Post-Industrial Methane should also emphasize that the role methane plays in the
2 determining global tropospheric ozone concentrations has been quantified only by chemistry-climate
3 model simulations. That dependence is expected to be critically dependent upon the model-derived
4 global NO_x concentration distribution, and the model simulations of that NO_x distribution are quite
5 sensitive to parameterizations of many physical processes within the models. The parameterizations
6 have been tested by observation-model comparisons only to a limited extent, so their success in
7 realistically simulating the physical processes remains uncertain. Finally, the NO_x concentration
8 distribution is poorly characterized from the limited measurements available, and the measured
9 concentrations are often at or below the detection limit of the instruments making the measurements.
10 Thus, in my opinion, increasing methane may indeed increase global ozone concentrations, but due to
11 model uncertainties that relationship is uncertain. Conceivably increasing methane may decrease, rather
12 than increase, global ozone concentrations. The uncertainty regarding methane's role should be made
13 clear.
14

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1 Section 2.5.2.2 – Methodology: Strengths, Limitations and Uncertainties - discusses uncertainties in
2 model estimates of USB. The final concluding sentence is “As a single estimate, this study relies upon

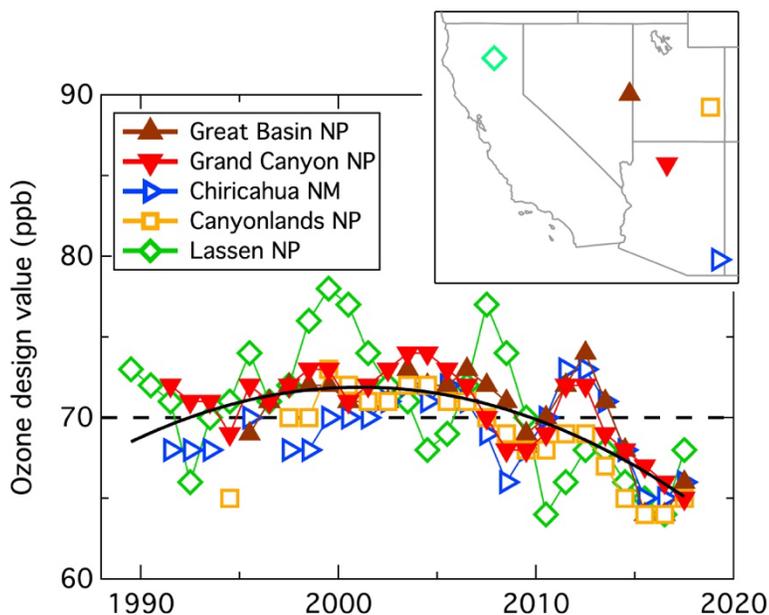


Figure 1. Ozone design values recorded at five relatively isolated CASTNET sites in the southwestern U.S. (Data from EPA's AQS data archive (<https://www.epa.gov/aqs>)).

2 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.

25

26

27 Figures 2.16 and 2.17 are informative plots. Evidently the minimum and maximum that are given are not
28 minimum or maximum simulated on any day in each season, but are instead the minimum and
29 maximum mean MDA8 O₃ concentration simulated for any grid cell in the domain. This should be
30 clarified.

31

32 Figure 2-22 seems to indicate that MDA8 ozone from natural sources can exceed 70 ppb on many days
33 in the western U.S. and even on some days in the eastern U.S. Does this not imply that natural sources
34 alone can give an ozone design value larger than the current NAAQS of 70 ppb, at least in the western
35 U.S.? The right center panel of Figure 2-27 shows that this is indeed the case, with the maximum 4th
36 highest US background O₃ simulated day of 80 ppb. Does this not imply that it is impossible to reach the
37 current NAAQS of 70 ppb through domestic precursor emission controls only? Further, that figure
38 shows that ozone design values can be above ~60 ppb from US background ozone alone over much of
39 the western U.S. This map is roughly similar to the maps that I included in my response to questions
40 regarding the O₃ ISA, and are reproduced here as Figures 2 and 3. These three figures from two model

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1 calculations and one observational based analysis show how difficult it is to reach even a 70 ppb
2 NAAQS in large regions of the country. This issue deserves full discussion in this chapter. The final
3 conclusion of this section is a good start for this recommended full discussion: "...a combination of
4 Natural and Canada/Mexico contributions can lead to total USB between 60-80 ppb on specific days,
5".

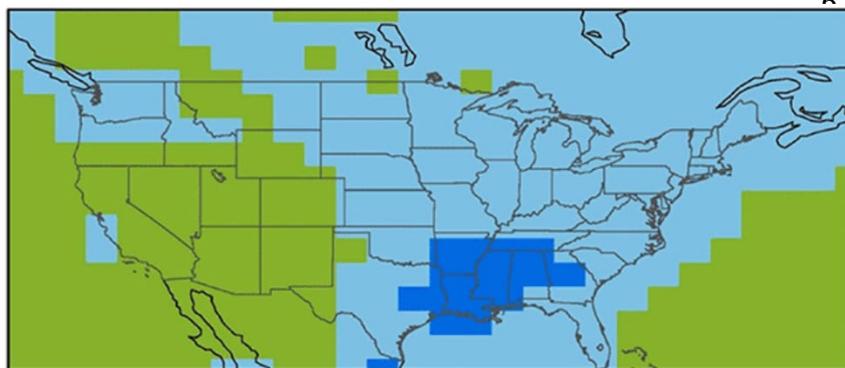


Figure 2. Annual 4th highest MDA8 O₃ in ppb from North American background (i.e., with North American anthropogenic precursor emissions set to zero) averaged over 2010–2014 from a GFDL-AM3 model simulation (Jaffe et al., 2018).

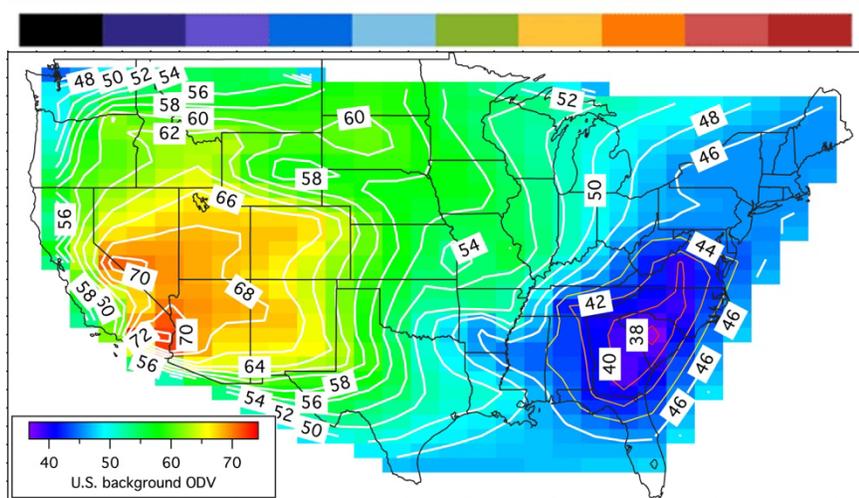


Figure 3. Ozone design values expected from U.S. background (i.e., with U.S. anthropogenic precursor emissions set to zero) in ~ 2015 derived from observations (D.D. Parrish, unpublished figure).

31
32 **Chapter 3 – Review of the Primary Standard**

- 33
- 34 • *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section*
35 *3.4.1) accurate and complete? If not, what additional information needs to be included?*

36
37 I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.
38

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- 1 • *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the*
2 *Current Standard (Section 3.4.2) accurate and complete? If not, what additional information*
3 *needs to be included?*
4

5 I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.
6

- 7 • *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality*
8 *Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be*
9 *included?*
10

11 I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.
12

- 13 • *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what*
14 *additional information needs to be included?*
15

16 I have no relevant expertise in evaluating exposure and risk, so I cannot respond to this question.
17

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

20 I have no relevant expertise in evaluating public health implications, so I cannot respond to this
21 question.
22

23 **Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses**
24

- 25 • *Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what*
26 *additional information needs to be included?*
27

28 Very limited summary data for each urban area are given in Table 3C-1. I have not independently
29 checked those data, but they appear to be accurate and complete.
30

- 31 • *Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete?*
32 *If not, what additional information needs to be included?*
33

34 This section simply describes the data which were downloaded from the EPA's Air Quality System
35 (AQS) database; the discussion appears to be accurate and complete.
36

- 37 • *Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1)*
38 *accurate and complete? If not, what additional information needs to be included?*
39

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1 I do not have experience with performing photochemical model simulations. To me the discussion of
2 CAMx appears accurate, as expected, since this section is simply a discussion of how a widely-used
3 photochemical model was setup for the application described in this Appendix.
4

5 One issue that is always relevant for model calculations is the accuracy of the emission inventory. A
6 paragraph discussing how the emissions assumed for this model compare with other measures of U.S.
7 emissions would provide useful information. For example, a quick comparison between the total
8 emissions in Table 3C-4 with the total emissions given in the pie charts in Figure 2-1 shows some
9 similarities and some surprising differences. For CO, both the anthropogenic and natural components are
10 in close agreement. For VOCs, the anthropogenic components agree well, but in the CAMx inventory
11 the biogenic VOCs are larger by about 11%. Surprisingly, the anthropogenic NOx emissions are about
12 20% smaller in the CAMx inventory. These differences are certainly within the uncertainty of the
13 inventories, but even these small differences may have an effect on the modeling results. The difference
14 in anthropogenic NOx emissions may be particularly important in this particular modeling study,
15 because NOx emissions are the parameter adjusted in the Air Quality Adjustments in Section 3C.5. A
16 parameter that modelers often use to explain features of atmospheric photochemistry is the VOC to NOx
17 ratio. In the CAMx inventory (Table 3C-4) this ratio (on a wt:wt basis) is about 5.1 compared to 3.9 in
18 the NEI Inventory (Figure 2-1), based on the total emissions. It would be useful to discuss the impact of
19 this difference in VOC to NOx ratio, along with any other significant uncertainties in the emissions that
20 might impact the results.
21

22 As second issue that affects the results of the modeling is the accuracy of the boundary conditions
23 calculated by the hemispheric version of the Community Multi-scale Air Quality model (H-CMAQ)
24 v5.2.1. These boundary conditions account for the majority of the ozone throughout the modeling
25 domain; thus, the accuracy of all of the results of this modeling exercise depends on the accuracy of the
26 boundary conditions. A comparison of the modeled ozone concentrations at CASTNET sites,
27 particularly in the western U.S. (as shown in Figure 1 above), would give an insightful indication of
28 their accuracy. A zero-out model run with all U.S. anthropogenic emissions set to zero should be
29 conducted to calculate U.S. background ozone, and the results compared with other determinations of
30 U.S. background ozone (also see maps in Figures 2 and 3 above).
31

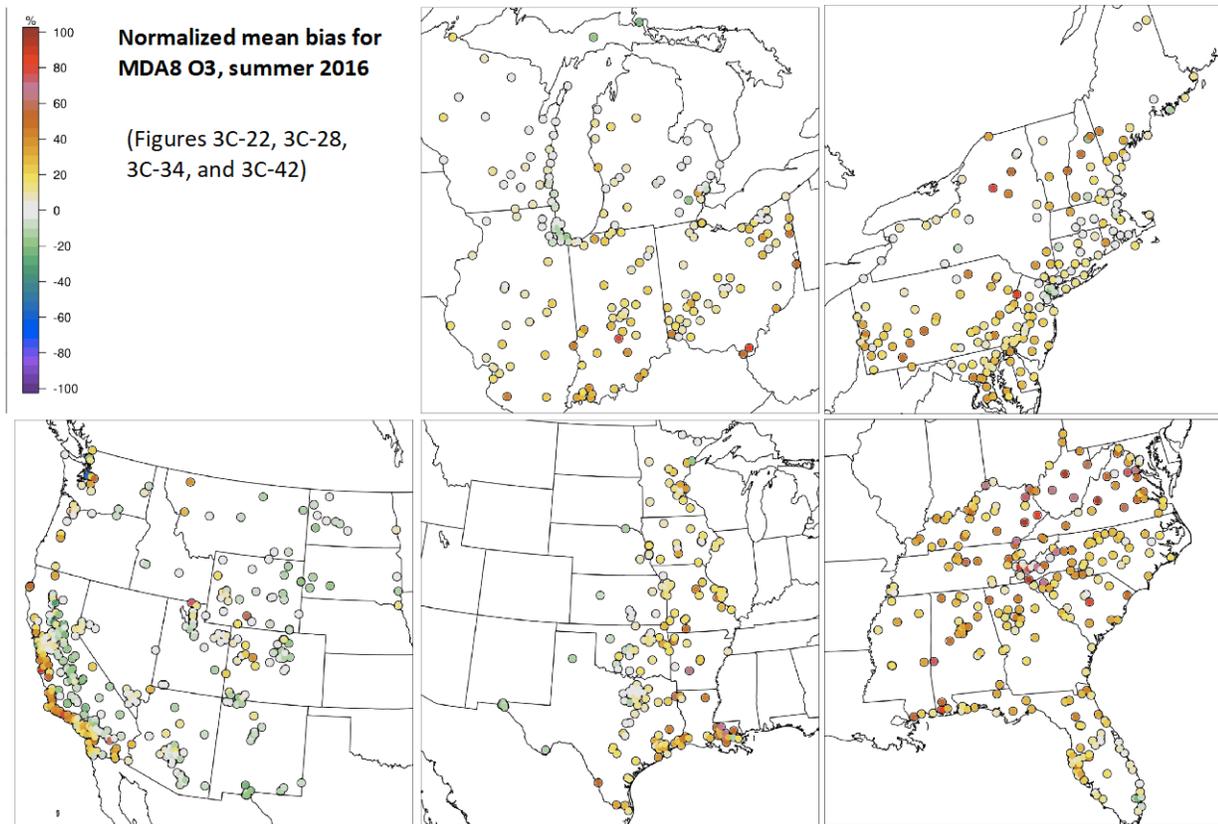
- 32 • *Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and*
33 *complete? If not, what additional information needs to be included?*
34

35 This section contains 33 pages with 13 Tables and 36 Figures, many with multiple panels. More
36 numbers and graphs are not needed for completeness, but a better synthesis of the results would be
37 useful. Figures could be combined to allow an easier approach to that synthesis. For example, the
38 following figure combines 5 figures from the report so that a reader can easily compare and contrast
39 results across the country. The discussion of these results could then be more concise and insightful.
40

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1



2

3

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

9

10 I am not an expert in modeling, so I cannot critique the modeling procedures described in this section. I
11 have not identified any inaccuracies or incompleteness in the description of the modeling. However, to
12 my mind this section is incomplete in two regards. First, an overview of the reasons for choosing the
13 emissions adjustments (NO_x emission reductions alone) used in this section should be given. Figure 3C-
14 48 is a flow diagram demonstrating the HDDM model-based O₃ adjustment approach. One part of Step
15 3 is to select emissions reductions to which sensitivities will be applied. How are these reductions
16 selected? Throughout this section, only NO_x emissions are reduced, but in the real world, anthropogenic
17 VOC emissions are reduced simultaneously with NO_x reductions. The introduction to this section
18 should give the reader some idea of what guided the choices made during this modeling exercise.
19 Second, a discussion of the likely uncertainties of the final results should be given.

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- 1
2
3
4
5
- *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?*

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

15
16 Apparently, there are some unrealistic results included in the summary plots and tables; I suggest that
17 they be removed. For urban areas that already had design values below 75 ppb in 2017, modeling was
18 done for NO_x emission **increases** necessary to **raise** the design values up to 75 ppb (Table 3C-19). This
19 may be a modeling exercise that is useful for completeness, but is simply confusing to at least this
20 reader. Figures like the left panel of Figure 3C-84 should not be included. Similarly, for the respective
21 panes in Figures 3C-91 through 3-114.

- 22
23
24
25
- *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?*

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

- 34
35
36
37
- *Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not, what additional information needs to be included?*

38 This section has an effective and complete presentation of the results. In each of the eight panels in
39 Figures 3C-107 through 3C-114, I suggest that the average, population-weighted annual 4th highest
40 MDA8 O₃ or May-September mean MDA8 O₃ be indicated in annotations.

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1
2 In my opinion, the summary sentence for this section is inadequate. It currently reads “In summary,
3 these figures show that using the CAMx/HDDM adjustment methodology, peak O₃ concentrations are
4 reduced in urban areas with large domain wide reductions in U.S. anthropogenic NO_x emissions.” I
5 think that a statement should be added to the effect that the total population weighted average ambient
6 MDA8 ozone concentrations decrease with emission reductions designed to reduce the annual 4th
7 highest MDA8 O₃ concentration. The success of the U.S. program in reducing ambient ozone
8 concentrations requires emphasis, regardless of whether the NAAQS has been, or even can be, reached
9 in some urban areas.

10
11
12 **Questions from Dr. Sabine Lange**

13
14 Air Quality

15
16 *1) Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have*
17 *demonstrated that in an area where peak daily ozone concentrations have decreased over time,*
18 *over the same period of time the lowest daily ozone concentrations have also decreased (due to*
19 *the NO_x disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are*
20 *your thoughts about the change of annual average ozone concentrations (which tend to be the*
21 *focus of epidemiology studies) with decreases in annual peak ozone concentrations?*
22

23 The general situation exemplified in Figure 1 is more or less typical of the temporal evolution of urban
24 ozone concentration distributions, where maximum daily 8-hour average (MDA8) ozone concentrations
25 have decreased, but the minimum MDA8 values have increased. This causes the distribution of MDA8
26 ozone concentrations to narrow, as shown in the figure. The cause of the increase in the minimum
27 MDA8 ozone concentrations is a reduction in fresh NO emissions in the urban area. The effect of these
28 emissions on days of low photochemical activity is for NO to react with ozone, forming NO₂. Thus,
29 between the early 2001-2003 period and the later 2013-2015 period, on days of low photochemical
30 activity the MDA8 ozone concentrations have increased but the NO₂ concentrations have decreased.
31 Since the mean and median MDA8 have not changed significantly over this time interval, it may well be
32 that the annual average ozone concentrations have not changed much. The possibility that annual
33 average ozone concentrations have not changed, but that NO₂ concentrations have decreased, would be
34 important to consider in the interpretation of epidemiology studies that focus on annual average ozone
35 concentrations.

36
37 Epidemiology
38

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- 1 2) *Is an epidemiology study with higher statistical power (sample size) innately more protected*
2 *against problems of confounding, error, and bias, than an epidemiology study with lower*
3 *statistical power (sample size)?*
4

5 I have no relevant epidemiological expertise, so I cannot respond to this question.
6

- 7 3) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4*
8 *(Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are*
9 *generally assessing the associations between ambient ozone and specific health outcomes and*
10 *are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg. 3-*
11 *40 and pg. 3-43). Do you think that this statement is correct? If so, is this statement generally*
12 *true of air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific*
13 *to ozone, then should this caveat always be considered when evaluating exposure concentrations*
14 *associated with these types of epidemiology studies?*
15

16 I have no relevant epidemiological expertise, so I cannot respond to this question.
17

18 Exposure-Response Modeling
19

- 20 4) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that “In recognition of the lack of*
21 *data for some at risk groups and the potential for such groups, such as children with asthma, to*
22 *experience lung function decrements at lower exposures than healthy adults, both models*
23 *generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations*
24 *investigated in the controlled human exposure studies.” Is assuming a lack of threshold in an*
25 *exposure-response relationship a standard method for considering potential at-risk populations*
26 *that may not have been characterized in an exposure-response assessment?*
27

28 I have no relevant health effects expertise, so I cannot respond to this question.
29

- 30 5) *The EPA also notes in this section that there is a lack of information about the factors that make*
31 *people more susceptible to ozone-related effects, and that the risk assessment could therefore be*
32 *underestimating the risk. However, the exposure-response model used to estimate the risk of lung*
33 *function decrements uses those people in the health population with a greater response to ozone*
34 *than the mean response (i.e. that fraction of the people in controlled human exposure studies*
35 *who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration*
36 *for more susceptible people in the population?*
37

38 I have no relevant health effects expertise, so I cannot respond to this question.
39
40

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1 **Questions from Dr. Corey Masuca**
2

3 ***1) 2.1. Ozone and Photochemical Oxidants in the Atmosphere***
4

5 *How sound science is this mechanism of ozone transfer between the stratosphere and the troposphere?*
6

7 The scientific evidence that ozone transfer from the stratosphere to the troposphere occurs in
8 stratospheric intrusions associated with tropopause folds is very strong. The science that underlies our
9 understanding of the injection of stratospheric intrusions into the troposphere, their transport within the
10 troposphere, and their dispersion into the background troposphere is also strong, because it is based on
11 our understanding of meteorology, which has a long history of extensive research. The work by
12 Langford et al. (2018) is a good example of the state-of-the-art of our ability to use observations and
13 transport modeling to characterize the impact of a specific stratospheric intrusion event.
14

15 A second mechanism for stratosphere to the troposphere exchange occurs over northern mid-latitude
16 continents, where strong convection associated with thunderstorms penetrates to the stratosphere, and
17 brings stratospheric air into the troposphere. I believe that less research has been devoted to this
18 mechanism, but on a global scale it is thought to have a smaller impact than tropopause folding events.
19 Ultimately, it would be valuable to be able to accurately quantify the contribution that ozone from the
20 stratosphere makes to observed surface ozone at any particular time and place; the science is not yet
21 advanced enough for this to be possible. Models can provide partial answers (e.g., Langford et al., 2017)
22 but the accuracy of those answers is not well quantified.
23

24 ***2) 2.3.1 Ambient Air Monitoring Requirements and Monitoring Networks***
25

26 *While a number of types of sites are mentioned in this section such as PAMS, NCore, CASTNET,*
27 *National Park Service (NPS), and Special Purpose Monitors (SPMs), what about Near Road Monitoring*
28 *Sites, especially for NO_y?*
29

30 As of September, 2019, there were apparently 82 Near Road Monitoring Sites in many states throughout
31 the U.S. (<https://www3.epa.gov/ttnamti1/nearroad.html>) that operated for at least some period of time.
32 The goal of this network is to quantify NO₂ concentrations in the near field of vehicle emissions. As far
33 as I know, there is no emphasis on measurement of NO_y at these sites. Adding a brief discussion of this
34 network to Section 2.3.1 would be useful.
35

36 ***3) 2.3.2 Data Handling Conventions and Comparisons for Determining Whether Standards Are Met***
37

38 *There is a reference to the hourly concentrations being utilized to compute 8-hour averages. Is this*
39 *short-term 8-hour rolling average consistent with short-term actual and scientific studies?*
40

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1 The maximum of the 8-hour rolling averages (MDA8) recorded on a given day is useful for scientific
2 studies. On sunny days that usually experience the largest ozone concentrations, this average generally
3 characterizes the ozone concentration during the period of the day when 1) the largest ozone
4 concentrations have accumulated, and 2) when the convective boundary layer is well developed.
5

6 **4) 2.4.3 Diurnal Patterns**

7
8 *While this section refers diurnal patterns of relative ozone concentrations between day and night, are*
9 *these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant*
10 *weather conditions? What about the effects on topography/geography in determining diurnal patterns?*
11

12 The diurnal pattern of ozone at surface sites is driven by several processes. The influence of each factor
13 at a particular site varies depending upon the characteristics of each site, so each site has its own
14 characteristic diurnal pattern.
15

16 At most sites in relatively flat terrain, the most important factor is usually the evolution of the
17 convective boundary layer. At night during relatively calm wind periods, the boundary layer is shallow
18 (nominally 10s of meters to ~100m). Ozone is lost to surfaces, and this surface deposition can reduce
19 surface ozone to low concentrations within this shallow layer, which includes the ozone monitor. In
20 areas with significant surface NO_x emissions, reaction of ozone with freshly emitted NO also
21 contributes to the depletion of near-surface ozone. After sunrise, solar radiation heats the surface,
22 initiating convection that in the morning hours increases the depth of the boundary layer by entraining
23 air from aloft. This air was above the nocturnal boundary layer, so its ozone concentration has not
24 changed appreciably overnight; surface ozone concentrations increase due to this entrainment.
25

26 A second important factor is photochemical production of ozone from precursors contained in the
27 boundary layer. The contributions to the ozone increase from entrainment of air aloft and photochemical
28 production within the boundary layer are not easily distinguished from measurements, since both
29 processes are occurring simultaneously.
30

31 A third factor is advection (horizontal transport) of air to the site. If there is an urban area upwind, then
32 rural ozone may increase later in the afternoon, when urban pollution ozone is finally advected to the
33 site.
34

35 These three factors are each affected by temperature during the day (with higher temperature generally
36 favoring both faster boundary layer growth and faster photochemical ozone production) and
37 meteorology including the degree of stagnation (which affects boundary layer growth and advection).
38

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

4
5 Thus, it is difficult to give a simple explanation of diurnal ozone patterns. The discussion of Figure 2-10
6 in this section gives a reasonably accurate overview.

7
8 **5) Background Ozone**

9
10 *There, in general appears to be a lot of discussion about background ozone concentrations from*
11 *transport and natural sources. However, are most salient ozone concentrations more localized and from*
12 *anthropogenic sources?*

13
14 The short answer is no. As I noted in my comments on Section 1.8 of the ISA on U.S. background ozone
15 concentrations, at present U.S. background ozone contributes the majority of urban ozone
16 concentrations, even on most days when ozone exceeds the NAAQS. The figures in Section 2.5 of the
17 PA agree with this statement. In my response to a question on background ozone that was posed during
18 the review of the ISA, I included two contour maps showing estimates of USB across the country, one
19 from a model calculation and one from an observational based analysis. They are reproduced above as
20 Figures 2 and 3. Broadly speaking the two maps agree that the ozone design value that would be
21 measured in the absence of U.S. anthropogenic emissions of ozone precursors would vary from ~40 ppb
22 to ~70 ppb, with the larger values in the southwest and the lower values in the southeast. During
23 exceedance episodes, the more localized ozone concentrations from anthropogenic sources can usually
24 be conceptually viewed as a relatively smaller contribution that raises the U.S. background ozone
25 concentration above the NAAQS.

26
27 *This section references the utilization of photochemical grid models due to the lack of ability to*
28 *characterize the origins of ozone and the ability to estimate the magnitude of background ozone.*
29 *However, how predictable are these photochemical models, especially given the highly photolytic and*
30 *relative instability of ozone in the atmosphere?*

31
32 The results from photochemical grid model simulations have poorly quantified uncertainties. However,
33 these uncertainties are relatively large compared to the margin between the NAAQS and the observed
34 ozone design values in most nonattainment areas of the country. For example, Jaffe et al. (2018)
35 estimates that the uncertainty in U.S. background ozone concentrations calculated by models is around
36 ± 10 ppb for seasonal mean values and higher for individual days. Attainment vs. nonattainment
37 decisions are often based on ozone concentration differences that are smaller than this uncertainty. The
38 U.S. EPA recognizes that the absolute ozone concentrations simulated by models have significant
39 uncertainties, so the use of Relative Response Factors (RRF) are recommended during the development
40 of state implementation plans (for example, see

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1 https://cfpub.epa.gov/si/si_public_record_report.cfm?Lab=NERL&dirEntryId=306790). The RRF
2 approach assumes that models can accurately calculate the response of ambient ozone concentrations to
3 precursor emission changes, even while the model cannot accurately calculate the absolute ozone
4 concentrations. In looking through the ozone ISA and PA, I find no discussion of the RRF approach,
5 which I believe is a major shortcoming of these documents.

6
7 *This section mentions that international emissions sources via transport mostly originate from*
8 *anthropogenic sources. However, is there a possibility that there can be international transports from*
9 *non-anthropogenic/biogenic sources?*

10
11 *Also, this section noticeably leaves out non-international, interstate transport of ozone.*

12
13 International transport from non-anthropogenic/biogenic sources is extremely important. Ozone from
14 stratospheric intrusions and ozone precursors from wild fires are two very important examples. I think
15 that the discussion of the U.S. background correctly focuses on the international transport because non-
16 international, interstate transport of ozone is adequately treated in the regional photochemical modeling.

17
18 **6) 2.5.1.6 Pre-Industrial Methane**

19
20 *There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance*
21 *of methane with respect to the formation of and consideration of ozone? Is a discussion on methane*
22 *warranted?*

23
24 Methane as a participant in atmospheric photochemistry and may well make a significant contribution to
25 U.S. background ozone concentrations. Section 2.5.1.6, which constitutes about 1 page of the 64-page
26 chapter, is I think warranted.

27
28 **References**

29
30 Jaffe D. A., et al. (2018) Scientific assessment of background ozone over the U.S.: Implications for air
31 quality management. *Elem. Sci. Anth.*, 6 56 doi.org/10.1525/elementa.309.

32
33 Langford, A. O., et al. (2017), Entrainment of stratospheric air and Asian pollution by the convective
34 boundary layer in the southwestern U.S., *J. Geophys. Res. Atmos.*, 122, 1312–1337,
35 doi:10.1002/2016JD025987.

36
37 Langford, A. O., et al. (2018). Coordinated profiling of stratospheric intrusions and transported pollution
38 by the Tropospheric Ozone Lidar Network (TOLNet) and NASA Alpha Jet experiment (AJAX):
39 Observations and comparison to HYSPLIT, RAQMS, and FLEXPART, *Atmos. Environ.*, 174, 1-
40 14, <https://doi.org/10.1016/j.atmosenv.2017.11.031>.

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13

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>.

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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.

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1 **4) 2.4.3 Diurnal Patterns**
2

3 *While this section refers diurnal patterns of relative ozone concentrations between day and night, are*
4 *these diurnal patterns solely (although mostly are) attributable to temperature? What about stagnant*
5 *weather conditions? What about the effects on topography/geography in determining diurnal patterns?*
6

7 EPA does a good job in summarizing information related to not only diurnal patterns, but also
8 regional patterns where specific weather conditions (such as stagnant weather patterns) and/or
9 topography could impact ozone concentrations (i.e., based on the selection of examples provided
10 as in Figures 2-10 and 2-11). While additional discussion could be included to specifically
11 address these points, the examples provided show a good range of different conditions that could
12 impact ozone concentrations spatially and regionally.
13

14 **5) Background Ozone**
15

16 *There, in general appears to be a lot of discussion about background ozone concentrations from*
17 *transport and natural sources. However, are most salient ozone concentrations more localized and from*
18 *anthropogenic sources?*
19

20 I appreciate that EPA includes a thorough discussion of background sources of ozone because in
21 some regions of the country, background ozone levels can be a significant contributor to overall
22 ozone levels, and this makes it challenging to meet increasingly more stringent NAAQS.
23 Understanding when and how much background ozone contributes to overall ozone levels will
24 help in attainment of the NAAQS.
25

26 *This section references the utilization of photochemical grid models due to the lack of ability to*
27 *characterize the origins of ozone and the ability to estimate the magnitude of background ozone.*
28 *However, how predictable are these photochemical models, especially given the highly photolytic and*
29 *relative instability of ozone in the atmosphere?*
30

31 I am not sufficiently familiar with the photochemical models to comment on this question.
32 *This section mentions that international emissions sources via transport mostly originate from*
33 *anthropogenic sources. However, is there a possibility that there can be international transports from*
34 *non-anthropogenic/biogenic sources?*
35

36 I agree that it is possible for international transport of biogenic precursors to also contribute, but
37 it may be more difficult to evaluate the contributions from these sources.
38

39 *Also, this section noticeably leaves out non-international, interstate transport of ozone.*
40

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1 I agree that this is an important issue that should be addressed.
2

3 **6) 2.5.1.6 Pre-Industrial Methane**
4

5 *There is a whole section devoted to long-lasting atmospheric methane. However, what is the importance*
6 *of methane with respect to the formation of and consideration of ozone? Is a discussion on methane*
7 *warranted?*
8

9 I am not sufficiently familiar with all the details regarding ozone chemistry, if it does play a
10 significant role in ozone formation, then I think it is appropriate for methane to be discussed.
11

12
13 **Questions from Dr. Sabine Lange**
14

15 Air Quality
16

17 *11) Multiple ozone chemistry analyses (e.g. Downey et al., 2015; Simon et al., 2012) have*
18 *demonstrated that in an area where peak daily ozone concentrations have decreased over time,*
19 *over the same period of time the lowest daily ozone concentrations have also decreased (due to*
20 *the NOx disbenefit aspect of ozone chemistry). An example is provided in Figure 1. What are*
21 *your thoughts about the change of annual average ozone concentrations (which tend to be the*
22 *focus of epidemiology studies) with decreases in annual peak ozone concentrations?*
23

24 EPA does acknowledge that “Reductions of NOX emissions are expected to result in a
25 compressed O3 distribution, relative to current conditions” (Draft Ozone PA, pg. 2-4),
26 and it looks like that is what is shown in Dr. Lang’s Figure 1. As Figure 1 shows,
27 however, this also means that there will be more days that experience somewhat higher
28 ozone concentrations, although potentially no days with levels that exceed very high
29 concentrations. With regards to how these changes should be interpreted for
30 epidemiology studies, I think the larger issue of how ambient levels relate to actual
31 personal exposures of ozone and how this impacts exposure measurement error in the
32 epidemiology studies is a more critical issue. In the PA, EPA acknowledge this important
33 source of uncertainty, and is one reason provided for not conducting the “epidemiology-
34 based” risk assessment.
35

36 Epidemiology
37

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

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1
2 The issue of statistical power is separate from issues related to confounding, errors and
3 bias. You can have a very large study that has serious confounding issues if these are not
4 controlled for (or are unmeasured). Similarly, large studies can be prone to selection bias,
5 exposure measurement errors, etc. Sample size (or statistical power) will affect whether
6 you are able to “detect” an effect, and is only one aspect of study quality (larger sample
7 sizes are preferred), but is separate from other issues of study quality, which are
8 associated with the study design, execution, and analyses methodology. That is, poor
9 study design, execution or poor methodology can lead to errors and biases.

10
11 *13) In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4*
12 *(Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are*
13 *generally assessing the associations between ambient ozone and specific health outcomes and*
14 *are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40*
15 *and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of*
16 *air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to*
17 *ozone, then should this caveat always be considered when evaluating exposure concentrations*
18 *associated with these types of epidemiology studies?*

19
20 I agree with this statement – the ambient data, whether from fixed-site monitors or from
21 modeling data are only surrogates of the actual personal exposures and any differences
22 contribute to exposure measurement errors. This statement is true for all air pollution
23 studies, not only ozone, and this caveat should be included for other air pollution
24 epidemiology studies.

25
26 Exposure-Response Modeling

27
28 *14) In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that “In recognition of the lack of*
29 *data for some at risk groups and the potential for such groups, such as children with asthma, to*
30 *experience lung function decrements at lower exposures than healthy adults, both models*
31 *generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations*
32 *investigated in the controlled human exposure studies.” Is assuming a lack of threshold in an*
33 *exposure-response relationship a standard method for considering potential at-risk populations*
34 *that may not have been characterized in an exposure-response assessment?*

35
36 This approach does not make sense to me. If asthmatics are truly more susceptible to the
37 effects of ozone, then it might be that the threshold for effects might be lower, but not
38 zero. Although data are limited, the data that are available do not indicate that asthmatics
39 are more susceptible than non-asthmatics to the effects of ozone. In fact, data are
40 inconsistent, with some studies indicating effects in asthmatics at elevated ozone

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1 exposures, but others showing no effects. For example, no effects on lung function were
2 observed in asthmatics compared to non-asthmatics at exposures to 400 ppb for 2 hours
3 (Alexis *et al.*, 2000) and 200 ppb for 2 hours (Mudway *et al.*, 2001).
4

5 Alexis, N; Urch, B; Tarlo, S; Corey, P; Pengelly, D; O'Byrne, P; Silverman, F. 2000.
6 "Cyclooxygenase metabolites play a different role in ozone-induced pulmonary function
7 decline in asthmatics compared to normals." *Inhal. Toxicol.* 12(12):1205-1224.
8

9 Mudway, IS; Stenfors, N; Blomberg, A; Helleday, R; Dunster, C; Marklund, SL; Frew,
10 AJ; Sandstrom, T; Kelly, FJ. 2001. "Differences in basal airway antioxidant
11 concentrations are not predictive of individual responsiveness to ozone: A comparison of
12 healthy and mild asthmatic subjects." *Free Radic. Biol. Med.* 31(8):962-974.
13

14 *15) The EPA also notes in this section that there is a lack of information about the factors that make*
15 *people more susceptible to ozone-related effects, and that the risk assessment could therefore be*
16 *underestimating the risk. However, the exposure-response model used to estimate the risk of lung*
17 *function decrements uses those people in the health population with a greater response to ozone*
18 *than the mean response (i.e. that fraction of the people in controlled human exposure studies*
19 *who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration*
20 *for more susceptible people in the population?*
21

22 The controlled human exposure studies that form the basis of the exposure-response
23 model are based on exposure circumstances that are highly unlikely to occur in the
24 general population, and in particular in susceptible population groups (i.e., heavily
25 exercising individuals exposed to elevated concentrations of ozone over extended periods
26 of time). Only outdoor workers are likely to experience the exposure conditions in these
27 studies. In addition, the results clearly indicate that only a small percentage of the study
28 volunteers (although generally healthy adults) had a statistically significant response to
29 ozone, and as noted by Dr. Lange, these responders likely represent people that are more
30 susceptible to ozone (particularly at lower ozone concentrations). Therefore, I agree that
31 the model already represents a very conservative estimation of ozone effects that are
32 likely to be protective of sensitive population groups.
33
34

35 **Questions from Dr. James Boylan**

36
37 **Chapter 2 – Air Quality**
38

- 39 • *Is the discussion on O₃ and Photochemical Oxidants in the Atmosphere (Section 2.1) accurate*
40 *and complete? If not, what additional information needs to be included?*

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- 1 • *Is the discussion on Sources and Emissions of O₃ Precursors (Section 2.2) accurate and*
2 *complete? If not, what additional information needs to be included?*
- 3 • *Is the discussion on Ambient Air Monitoring and Data Handling Conventions (Section 2.3)*
4 *accurate and complete? If not, what additional information needs to be included?*
- 5 • *Is the discussion on Ozone in Ambient Air (Section 2.4) accurate and complete? If not, what*
6 *additional information needs to be included?*
- 7 • *Is the discussion on Background O₃ (Section 2.5) accurate and complete? If not, what additional*
8 *information needs to be included?*
9

10 Overall, for the PA, the discussion of Air Quality seemed accurate and complete. As
11 noted by other CASAC members, inclusion of state-to-state transport of ozone and ozone
12 precursors could be included, in addition to a discussion of potential international
13 transport of non-anthropogenic precursors of ozone.
14

15 **Chapter 3 – Review of the Primary Standard**
16

- 17 • *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach (Section*
18 *3.4.1) accurate and complete? If not, what additional information needs to be included?*
- 19 • *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the*
20 *Current Standard (Section 3.4.2) accurate and complete? If not, what additional information*
21 *needs to be included?*
- 22 • *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality*
23 *Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs to be*
24 *included?*
- 25 • *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what*
26 *additional information needs to be included?*
- 27 • *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If not,*
28 *what additional information needs to be included?*
29

30 In general, the overall summary of the Review of the Primary Standard was adequate for
31 the PA. The modeling of the Population and Exposure Risk Assessment (which I only
32 briefly reviewed) appeared to be very extensive and thorough, although I did not see any
33 of the actual estimates of the individual exposures, which would have been interesting to
34 see. Also, it would be interesting to compare the modeled estimates to actual personal
35 exposure studies to provide some validation for the model (I did not see any discussion of
36 model validation).
37
38
39
40

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1 **Appendix 3C – Air Quality Data Used in Population Exposure and Risk Analyses**
2

- 3 • *Is the discussion on Urban Study Areas (Section 3C.2) accurate and complete? If not, what*
4 *additional information needs to be included?*
5 • *Is the discussion on Ambient Air Ozone Monitoring Data (Section 3C.3) accurate and complete?*
6 *If not, what additional information needs to be included?*
7 • *Is the discussion on Comprehensive Air Quality Model with Extensions (CAMx) (Section 3C.4.1)*
8 *accurate and complete? If not, what additional information needs to be included?*
9 • *Is the discussion on Evaluation of Modeled Ozone Concentrations (Section 3C.4.2) accurate and*
10 *complete? If not, what additional information needs to be included?*
11 • *Is the discussion on Air Quality Adjustment to Meet Current and Alternative Air Quality*
12 *Scenarios (Section 3C.5) accurate and complete? If not, what additional information needs to be*
13 *included?*
14 • *Is the discussion on Interpolation of Adjusted Air Quality using Voronoi Neighbor Averaging*
15 *(Section 3C.6) accurate and complete? If not, what additional information needs to be included?*
16 • *Is the discussion on Results for Urban Study Areas (Section 3C.7) accurate and complete? If not,*
17 *what additional information needs to be included?*
18

19 In general, these sections of the PA appeared to be adequate and complete. I did not
20 review in detail to assess whether the information is accurate, as that would be beyond
21 my available time and expertise. The results and discussion seemed appropriate.
22
23
24

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1 **Dr. Duncan Thomas, University of Southern California**

2 **Questions from Dr. Sabine Lange:**

3
4 Air Quality

5
6 Not my area of expertise.

7
8 Epidemiology

- 9
10 1) *Is an epidemiology study with higher statistical power (sample size) innately more protected*
11 *against problems of confounding, error, and bias, than an epidemiology study with lower*
12 *statistical power (sample size)?*

13
14 **Response:** No. Sources of selection, information, and confounding biases could
15 potentially affect any study, irrespective of sample size (or power). That said, very large
16 studies conducted by highly experienced investigators generally make every effort to
17 address such problems in the design and analysis and would discuss these issues in their
18 publications. Also, studies of individual-level data may have access to more information
19 to address bias than meta-analyses or aggregate-level studies.

- 20
21 2) *In section 3.3.3 (Exposure Concentrations Associated with Effects) and section 3.3.4*
22 *(Uncertainties in the Health Effects Evidence), the EPA notes that the epidemiology studies are*
23 *generally assessing the associations between ambient ozone and specific health outcomes and*
24 *are not investigating the details of the exposure circumstances eliciting these effects (e.g. pg 3-40*
25 *and pg 3-43). Do you think that this statement is correct? If so, is this statement generally true of*
26 *air pollution epidemiology studies, or is it peculiarly specific to ozone? If it is not specific to*
27 *ozone, then should this caveat always be considered when evaluating exposure concentrations*
28 *associated with these types of epidemiology studies?*

29
30 **Response:** The two statements cited are generally correct and apply broadly to air
31 pollution epidemiology studies, not just ozone. Most epidemiologic studies are based on
32 measurements of ambient pollution levels, which are readily available. For some
33 pollutants, indoor sources or penetration from outdoor sources, local variation in
34 pollutant concentrations, time-activity patterns, etc., can be important sources of inter-
35 individual variation, which some studies have attempted to quantify by, for example,
36 personal monitoring, microenvironmental measurements, exposure modeling, GPS or
37 accelerometer instruments, etc., but such studies are expensive and may be infeasible for

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1 large-scale epidemiologic studies. Since the statements queried do apply to ozone studies,
2 I don't see than any particular caveats are needed to point out the generality of this issue.

3
4 Exposure-Response Modeling

- 5
6 3) *In section 3.4.4 (Key Uncertainties) of this PA, the EPA notes that "In recognition of the lack of*
7 *data for some at risk groups and the potential for such groups, such as children with asthma, to*
8 *experience lung function decrements at lower exposures than healthy adults, both models*
9 *generate nonzero predictions for 7-hour concentrations below the 6.6-hour concentrations*
10 *investigated in the controlled human exposure studies." Is assuming a lack of threshold in an*
11 *exposure-response relationship a standard method for considering potential at-risk populations*
12 *that may not have been characterized in an exposure-response assessment?*

13
14 **Response:** As I pointed out in earlier rounds of questions, the exact shape of a dose-
15 response relationship at low doses, including the existence or not of a threshold, is
16 difficult if not impossible to determine from feasible-sized epidemiologic studies. Hence,
17 the default analysis model generally assumes low-dose linearity (or log-linearity
18 depending on the form of the outcome variable); see for example the classic paper by
19 Crump, Hoel, Langley, and Peto (1976) I previously cited. This would be true for either
20 main effects in the whole population or for effect modification in potentially sensitive
21 subpopulations, to the extent that the necessary data on individuals are available. The
22 question of effects below the current standard is particularly important, and especially for
23 highly sensitive groups; to the extent that such data exist, any demonstrable low-dose
24 associations should be considered in revising the standard, whether or not the assumption
25 of low-dose linearity or thresholds can be tested.

- 26
27 4) *The EPA also notes in this section that there is a lack of information about the factors that make*
28 *people more susceptible to ozone-related effects, and that the risk assessment could therefore be*
29 *underestimating the risk. However, the exposure-response model used to estimate the risk of lung*
30 *function decrements uses those people in the health population with a greater response to ozone*
31 *than the mean response (i.e. that fraction of the people in controlled human exposure studies*
32 *who had FEV1 responses >10%, 15%, or 20%). Does this method already include consideration*
33 *for more susceptible people in the population?*

34
35 **Response:** This question appears to relate more to controlled human exposure studies
36 than to epidemiologic studies but does seem to be a reasonable approach for getting a
37 handle on inter-individual variability in susceptibility in that context. Obviously, the
38 slope of an exposure-response relationship in the general population will underestimate
39 risk for more sensitive individuals, or more importantly, for identifiable subgroups. Of
40 course, there are other characteristics than lung function (e.g., genetic variants,

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1 age/gender, baseline health status, etc.) that could influence sensitivity of ozone or other
2 pollutants. To the extent that the necessary data are available, most epidemiologic studies
3 have reported variation across quantifiable subgroups, and given EPA's mandate to
4 provide adequate protection to such groups as well as to the entire population should be
5 taken into consideration in revising standards.
6
7

8 **Questions from Dr. James Boylan**

9
10 ***Chapter 2 – Air Quality***

11
12 Not my area of expertise.

13
14 ***Chapter 3 – Review of the Primary Standard***

- 15
16 • *Is the discussion on Exposure and Risk Conceptual Model and Assessment Approach*
17 *(Section 3.4.1) accurate and complete? If not, what additional information needs to be*
18 *included?*
19 • *Is the discussion on Population Exposure and Risk Estimates for Air Quality Just Meeting the*
20 *Current Standard (Section 3.4.2) accurate and complete? If not, what additional information*
21 *needs to be included?*
22 • *Is the discussion on Population Exposure and Risk Estimates for Additional Air Quality*
23 *Scenarios (Section 3.4.3) accurate and complete? If not, what additional information needs*
24 *to be included?*
25 • *Is the discussion on Key Uncertainties (Section 3.4.4) accurate and complete? If not, what*
26 *additional information needs to be included?*
27 • *Is the discussion on Public Health Implications (Section 3.4.5) accurate and complete? If*
28 *not, what additional information needs to be included?*
29

30 **Response:** I found the passages that I read to be accurate and complete, to the best of my
31 knowledge.
32

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

34
35 Not my area of expertise.
36
37

38 **Questions from Dr. Corey Masuca**

39
40 None of these are in my area of expertise.