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Integrated Science Assessment (ISA) for Ozone and Related Photochemical Oxidants | US EPA

Proceedings for the Ozone National Ambient Air Quality Standards Science and Policy Workshop

Office of Research and Development, Center for Public Health and Environmental Assessment

Office of Air and Radiation, Office of Air Quality Planning and Standards

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By
Office of Research and Development
Center for Public Health and Environmental Assessment

Office of Air and Radiation
Office of Air Quality Planning and Standards

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Introduction

The last statutory periodic review of the air quality criteria and National Ambient Air Quality Standards (NAAQS) for ozone (O_3) and related photochemical oxidants was completed in 2020. In December 2020, the EPA issued its final decision to retain the existing O_3 NAAQS without revision. In October 2021, the U.S. Environmental Protection Agency (EPA) announced a reconsideration of the December 2020 decision. As part of the reconsideration, the EPA established a Clean Air Scientific Advisory Committee (CASAC) Ozone Review Panel, which provided advice to the EPA Administrator on science and policy documents through the CASAC. After carefully considering the CASAC's advice, the Administrator announced a new review of the O_3 NAAQS to ensure the standards reflect the most current, relevant science. The EPA is incorporating the ongoing reconsideration into the new review of the O_3 NAAQS and the underlying air quality criteria.

The new review of the O_3 NAAQS and air quality criteria was announced in August 2023. As part of the planning phase of this review, the EPA held a virtual public workshop May 13–16, 2024, to inform planning for the new review of the air quality criteria and the primary (health-based) and secondary (welfare-based) O_3 NAAQS. This workshop provided the EPA with an opportunity to receive input and advice on key science and policy issues for the review.

Participants invited to the workshop included experts internal and external to the EPA. These experts represented a variety of disciplines, including epidemiology; controlled human exposure studies; animal toxicology; ecology; statistics; biological, environmental, and physical sciences; atmospheric and climate science; human exposure science; and risk analysis. Workshop participants were invited to review several documents developed in the last review of the O_3 NAAQS and from the reconsideration. They were asked to highlight significant new and emerging policy-relevant research on O_3 and related photochemical oxidants and to discuss how new evidence can build on the analyses and scientific findings from the last review of the O_3 NAAQS.

Workshop discussions will inform the development of planning and assessment documents intended to serve as the foundation for the Agency's current review of the O_3 NAAQS. These documents will include the Integrated Review Plan, which will highlight the key policy-relevant issues and summarize anticipated assessment approaches; the Integrated Science Assessment, which will summarize and assess the most policy-relevant scientific evidence and make key science judgments; and quantitative air quality, risk, and exposure analyses, as warranted.

This document is intended to serve as a high-level summary of important topics discussed during the four-day workshop and to document new, potentially relevant research identified over the course of the workshop.

Each session was organized by topics that included a series of discussion questions for the panel of subject matter experts to discuss. Following each session was a question-and-answer period, in which the participants and the public could offer additional thoughts and topic-related questions or scientific literature.

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Acronyms and Abbreviations

Abbreviation	Term
AgMIP	Agricultural Model Intercomparison and Improvement Project
AI/ML	artificial intelligence and machine learning
CAA	Clean Air Act
CASAC	Clean Air Scientific Advisory Committee
CHAD	Consolidated Human Activity Database
CMAQ	Community Multiscale Air Quality Model
COVID	coronavirus disease
CPHEA	Center for Public Health and Environmental Assessment
CTM	chemical transport model
EJ	environmental justice
EPA	Environmental Protection Agency
FACE	free-air carbon dioxide enrichment
FIA	forest inventory analysis
HAP	hazardous air pollutants
hrs	hours
ISA	Integrated Science Assessment
MCC	multi-country multi-city
NPS	National Park Service
NO	nitric oxide
NO_2	nitrogen dioxide
NO_X	nitric oxide and nitrogen dioxide
O_3	ozone
OAR	Office of Air and Radiation
ORD	Office of Research and Development
OTC	open top chamber
PM	particulate matter
Ppb	parts per billion
RBL	relative biomass loss
REA	Risk and Exposure Assessment
RF	radiative forcing
SME	subject matter expert
SOF	stomatal ozone flux
USDA	United States Department of Agriculture
U.S.	United States
VNA	Voronoi Neighbor Averaging
VOC	volatile organic compound
VCP	volatile chemical product

Summary of Sessions and Questions

Monday, May 13, 2024

Purpose of Meeting

At the start of the workshop, the EPA noted for the audience the purpose of the workshop was to discuss policy-relevant science that will inform the EPA's current review of the air quality criteria and the NAAQS for O_3 and related photochemical oxidants. Workshop participants were asked to discuss recent science and key policy issues on O_3 and related photochemical oxidants. Input from this workshop will be considered during subsequent steps of the O_3 NAAQS review process.

Introduction to the NAAQS

The NAAQS are intended to protect the public health and public welfare against harmful effects of exposures to the "criteria" air pollutants. The criteria pollutants include O_3 and related photochemical oxidants, carbon monoxide, oxides of nitrogen, particulate matter, lead, and oxides of sulfur. The EPA establishes and periodically reviews NAAQS under Sections 108 and 109 of the Clean Air Act (CAA). Section 109(b)(1) of the CAA defines primary NAAQS as standards "the attainment and maintenance of which in the judgment of the Administrator, based on such [air quality] criteria and allowing an adequate margin of safety, are requisite to protect the public health." Under Section 109(b)(2), a secondary NAAQS must "specify a level of air quality the attainment and maintenance of which in the judgment of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of [the] pollutant in the ambient air." The first Air Quality Criteria for Photochemical Oxidants document was issued in 1970 and the first NAAQS for photochemical oxidants was published in 1971.

The three-phased NAAQS review process involves planning, assessment, and decision-making. The planning phase includes this type of workshop and the development of an Integrated Review Plan. The assessment phase includes development of an Integrated Science Assessment (ISA), a Policy Assessment (PA) and, as warranted, quantitative air quality, risk, and exposure analyses. The decision-making phase typically consists of a proposed decision, interagency review, public comments, and a final decision. The O_3 NAAQS were last revised in 2015 and then retained in the 2020 decision.

Session 1: Characterizing O_3 Chemistry and Transport, Air Quality Patterns, and O_3 as a Greenhouse Gas

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Anne Barkley, U.S. EPA; Olivia Clifton, NASA-GISS and Columbia University

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They noted that this session would focus on atmospheric science and climate effects. They provided background information on tropospheric O_3 exposures (background and non-background exposures). Tropospheric O_3 is formed from photochemical reactions of nitrogen oxides (NO_X) with volatile organic compounds (VOCs); background O_3 is sourced from stratospheric intrusions, international transport, wildfires, lightning, global methane, and biogenic precursors. Research advances presented in the 2020 O_3 ISA emphasized the emergence of winter O_3 events, the impact of the ENSO cycle, the reduction of days of O_3 concentration extremes, and climate impacts on global average surface temperatures. Additionally, a 2022 Draft Policy Assessment included knowledge gaps (e.g., photochemical modeling at high spatial and temporal resolutions, atmospheric chemistry and O_3, seasonal and geographic variations of O_3 precursors, MDA8 and W126, and the magnitude of climate system responses besides temperature).

Topic 1: O_3 Chemistry and Transport and Resulting Concentration Patterns

Discussion Question:

Since the last review, what new information is available and what are the most significant advancements in theoretical chemistry, kinetics and smog chamber work, field experiments, ambient monitoring, satellite retrievals, and numerical modeling that improve our current understanding of O_3 production and transport? What are the implications of this new information? Is there newly available evidence that indicates the importance of photochemical oxidants other than O_3 regarding abundance in ambient air?

Lead discussants: Sally Pusede, University of Virginia; Havala Pye, U.S. EPA

- Precursor sources are changing: NO_X emissions are decreasing as vehicle and power plant emissions decrease and soil NO_X could be becoming a more significant source. VOC emissions are changing as volatile chemical products and fire emissions replace vehicle and industrial emissions. As a result, VOC emissions are also becoming more oxygenated.
- Because of these decreasing vehicle and power plant emissions, NO_X-limited chemistry is becoming more important and better understood. COVID lockdowns have offered glimpses of this NO_X-limited future. Also, new aerosol reactions, such as particulate nitrate photolysis, have been identified that control chemistry in addition to VOCs. As wildfires have increased, NO_X reactivity has become increasingly influenced by VOCs emitted from wildfires, which contain more oxygen than traffic-related VOCs; this NO_X fire chemistry is also becoming better understood.
- Urban NO_2 concentrations have declined for decades, but this decline has slowed recently.
- Hydrotrioxides are an important oxidant species.
- Correctly forecasting the highest O_3 days remains a challenge.
- Wildland fire NO_X emissions are increasing. It is challenging to track O_3 in smoke as wildfire smoke interacts with urban air; O_3 formation chemistry from precursors within wildfire smoke plumes is better understood than the chemistry of O_3 formation resulting from the interaction

of O_3 precursors in wildfire plumes with O_3 precursors and other pollutants in urban air. Suggestion: More research is needed into how wildfire smoke interacts with urban airsheds and the resulting implications for urban O_3.

- Work is increasing to inform environmental justice considerations with finer spatial resolution data.
- O_3 concentrations in ambient air are a function of chemical O_3 production (from precursor sources of VOCs and NO_X), loss (through chemical reactions and deposition), and transport. The experts suggested examining literature on precursor source emissions, formation and loss chemistry, and atmospheric deposition, as they are most highly relevant for the current NAAQS review and report remarkable changes in the processes influencing ambient O_3 concentrations and our understanding of them since the previous O_3 NAAQS review (as discussed in next bullets).
- Concerning NO_X precursor sources, the relative contribution of motor vehicles and power plants to NO_X emissions has decreased, resulting in 1) an increased sensitivity of O_3 production to NO_X concentration, and 2) a larger contribution of NO_X from soils and wildfires, which is relevant to O_3 production and control because of different seasonal and diurnal patterns of emissions. Both consequences could influence both ambient O_3 concentrations and the relative effectiveness of different control strategies (e.g., VOC vs. NO_X emissions control).
- Concerning VOC precursor sources, recent research indicates that VOCs in U.S. ambient air are becoming more oxygenated because the relative contribution of oxygenated VOCs from volatile chemical products (solvents, consumer products, industrial products) and wildland fire emissions is increasing relative to motor vehicle VOC emissions, which are less oxygenated. How these changes affect the chemistry and extent of O_3 production is the subject of current research. Research on biogenic VOCs is underway and research on industrial VOC emissions is also needed.
- Concerning O_3 production and loss chemistry, hydrotrioxides were identified in 2022 as a previously ignored species with high potential for strong atmospheric oxidizing ability. Heterogeneous processes involving particulate matter, including particle uptake of hydroperoxy radicals, particulate nitrate hydrolysis, and aerosol nitrate photolysis, can also impact O_3 production in addition to VOCs and NO_X, especially in areas with high particulate matter levels. These processes are becoming better understood.
- Concentrations and emissions are increasingly resolvable at greater spatial resolution using satellites, mobile data, and models. This point is relevant to environmental justice-related inequalities that frequently occur at the neighborhood scale or smaller, and for better characterizing chemical processes that occur at a smaller scale than can be captured by typical chemical transport models, like fire plumes, urban neighborhoods, and near water bodies.
- O_3 deposition has become better understood and recent research shows that variability in O_3 deposition can alter O_3 concentrations on a scale similar to recently observed changes in NO_X emissions. Both emissions and deposition play a role in interannual variability in O_3 concentrations as key details of dry deposition processes—including important pathways not involving leaf stomata and the relationship of deposition to meteorology and biophysics—have become better understood.
- Chemical transport models used to predict O_3 concentrations continue to improve. CMAQ, a widely used model for O_3 prediction, generally underpredicts O_3 from January to May and

overpredicts O_3 from July to September, and it also generally underpredicts O_3 in the western United States and overestimates O_3 in the eastern United States. Improvements are possible as some of the research on physical and chemical processes described above is incorporated into future development.

- Major methodological advances have occurred in artificial intelligence and machine learning approaches that can help us understand and predict O_3 concentrations, including bias correction (to nudge predictions closer to observations), process simulation (speeding up slow parts of models without sacrificing accuracy), and improved spatial resolution (to the sub-km scale).
- The decrease in precursor source emissions described above has led to a compression of the O_3 concentration distribution in the United States, with fewer days of extremely high or low concentrations, as well as to changes in spatial, seasonal, and diurnal patterns and in some cases to divergent responses between different O_3 metrics (e.g., those that are based on peak concentrations used for public health protection vs. those based on weighted concentration distributions used for plant exposure).

Topic 2: Relationships between O_3 and Photochemical Oxidants Relevant for Health

Discussion Question:

What new information is available to inform how O_3 versus total oxidant exposure differs across spatial scales, particularly in urban areas where O_3 concentrations are low because of reactions with NO, and where environmental justice concerns are particularly important? What metrics are available to accurately describe the relationship between O_3 and total oxidant exposure; for example, could a combination of indicators be used?

Lead discussants: William Vizuete, University of North Carolina; Gail Tonnesen, U.S. EPA Region 8

- O_3 may not be a good indicator of total oxidant exposure because of complex chemical reactions with fresh emissions in urban airsheds that can result in very low O_3 concentrations despite heavy smog and high NO_X concentrations. Additionally, high O_3 concentrations with low NO_X concentrations can occur at sites in the U.S. Intermountain West at higher elevations (mostly in springtime) due to stratospheric O_3 intrusions. Therefore, an O_3 air quality metric may misrepresent the state of total oxidant exposure.

- One possible way to more accurately address total oxidant exposure would be to use other indicators, or a combination of indicators, including NO_2, HCHO, H_2O_2, RO_2, or black carbon. Currently, there is no set definition of which oxidants are included in total oxidant exposure. It may be up to the atmospheric chemistry community to define total photochemical oxidants and their relationship to O_3, which would enable health scientists to evaluate O_3 versus total oxidant exposure in health studies.

- Much more research is needed in this area, which may be limited by the availability of air quality monitoring networks. Model products, hybrid models, and remote sensing products may be helpful in bridging the monitoring gap and for estimating total oxidant exposure.

Question-and-Answer Session

What are your thoughts on O_x as an indicator?

- A study from Canada explored O_3 and NO_2. There are examples in the O_3 chemistry literature of using Ox in place of O_3. Ox should be the subject of future investigation.

Can the speakers talk about short-, medium-, and long(er)-lived compounds involved in complex O_3 chemistry (that have health implications) that tend to be either positively correlated with O_3 concentration (i.e., as O_3 increases these species also increase) or negatively correlated with O_3 concentrations (i.e., as O_3 is chemically lost these species increase)? This question is asked in the context of mixtures that people are exposed to and so perhaps should be considered in high(er) and low(er) **NO_X** ***regimes.***

- This question has two aspects: 1) understanding health effects from multipollutant mixtures and 2) measuring dynamic multipollutant mixtures as they photochemically age.
- Exposure assessment relies on existing data from satellite and ground concentrations, with retrospective modeling simulations playing a key role.
- There is concern about conditions in which O_3 concentrations can hit zero despite heavy pollution (e.g., winter, early morning).
- NO_X and O_3 will be correlated positively in some locations and negatively in others, which is important to consider when conducting health studies and using statistical methods because it could pose a challenge in data analyses.
- Measurements are also affected photochemically when oxidants are formed during the day; therefore, O_3 and NO_2 may not be the best indicators for total oxidants.
- Modeled spatial gradients may not be reliable for health impact assessment.

Do you have advice on how to recognize whether models are likely to be accurate or not?

- The gold standard is observation-based evaluation wherein modeling data are compared with data collected at observation stations.
- Errors made by models in one location will also be repeated in others.
- The use of machine learning models must be scrutinized in detail because of the errors they can produce.

Topic 3: Monitoring and Modeling Advances Relevant to Welfare

Discussion Question:

What recent advances have been made in monitoring (including satellites) and modeling ambient concentrations of O_3? How accurate are recently developed modeling approaches (including hybrid models that utilize data from satellites, land use information, ground-based monitors, etc.) at predicting O_3 emissions and ambient O_3 concentrations across locations (e.g., urban vs. rural, monitored vs. unmonitored)? What have these new tools and information contributed to characterizing and understanding how (e.g., wildfires, oil and gas operations, intercontinental transport) contribute to ambient O_3 concentrations, particularly in the west and intermountain west?

Lead discussants: Dan Goldberg, George Washington University; Heather Simon, U.S. EPA

- O_3 satellite retrievals are a work in progress, including improvements in vertical column data, spatial resolution, emissions estimates, precision, and uncertainty. Useful satellite-based indicators have evolved, including using formaldehyde as a proxy for O_3 and the formaldehyde-to-NO_X ratio to track increasingly NO_X-limited conditions. Further improvements in precision and spatial and temporal resolution are anticipated with the recent launch of the TEMPO satellite.
- Air quality modeling has improved. Improved understanding of relevant sources, such as volatile chemical products, wildfires, oil and gas operations, agricultural soil, and discoveries in

chemistry, such as aerosol nitrate photolysis, are becoming more complete and better represented in air quality models. Other notable modeling improvements include in-line lightning and biogenic emissions and integrating multiscale meteorology and transport in CMAQ, assimilation of satellite data into global models, characterization of dry deposition, and development of machine learning approaches.

- Advancements in ground-based monitoring systems include the NIST and EPA updates of the O_3 cross-section value used in UV-based O_3 analyzers and standard reference photometers (increasing by 1.2%), development of a ground-based network for vertical column measurements to complement satellite-based vertical column measurements, and application of LIDAR and ozonesondes for measuring vertical O_3 distributions.

- Several noteworthy datasets have become available that are based on recent modeling and measurement efforts, including a long-term dataset from EPA that ensures emissions characterization methods and model versions are consistent across the entire time series from 2002 to 2019, global O_3 data from the NASA GEOS Composition Forecast System and its European counterpart, and numerous U.S. field campaigns in various locations.

Topic 4: Background O_3 Concentrations

Discussion Questions:

There are various approaches to estimating background O_3, with different definitions currently or previously widely used within the U.S. air pollution research community. For instance, "U.S. background" is defined as the O_3 concentration that would occur if all U.S. anthropogenic O_3 precursor emissions were removed. "North American background" or "policy-relevant background" refers to the O_3 concentration that would occur in the United States in the absence of anthropogenic emissions in continental North America. In contrast, "baseline O_3" is defined as the measured O_3 concentration at rural or remote sites that have not been influenced by recent, local emissions (U.S. EPA, 2020).

What new information is available on characterizing or estimating background O_3 concentrations (e.g., including hybrid methods)?

Have new advances in monitoring and modeling contributed to characterizing sources and precursors (e.g., wildfires, intercontinental transport, stratospheric exchange) that contribute to background O_3 concentrations?

Is there new information on atmospheric transport, chemistry, and concentration trends that can be used to reduce uncertainties in seasonal or daily background O_3 estimates?

Lead discussants: Dan Jaffe, University of Washington; Barron Henderson, U.S. EPA

- Background O_3 from the stratosphere, soil, lightning, wildfires, biogenic sources, and international pollution remains an important NAAQS concern; wildfires are becoming an increasingly important contribution, with Canadian wildfires in the summer of 2023 largely responsible for a more than threefold increase over previous years in the number of days the current NAAQS level was exceeded.

- Characterization of O_3 using models could be enhanced through data assimilation, vertical mixing, and measurements.

- Greater understanding is needed of the impact of wildfire emissions and O_3 on urban air quality, particularly in the western United States where wildfire emissions can push an airshed over the NAAQS O_3 standard. Generalized additive models are helpful in estimating contributions of smoke to O_3 MDA8.

Future research should also focus on source apportionment (e.g., the Western and Eastern United States will have different primary O_3 drivers) and investigating the role of precursors such as methane and biogenic VOC emissions on O_3.

Topic 5: O_3 as a Greenhouse Gas

Discussion Questions:

- How have modeling studies conducted since the previous O_3 ISA changed its conclusions regarding the response of the climate system to O_3 impacts?
- What new information is emerging on the role of regional and seasonal variations in the atmospheric budgets of O_3 and therefore on its climate impacts?
- What new information is emerging on the impact of O_3 on the terrestrial ecosphere and its climate feedback?
- What is the role of precursors in the climate impacts of O_3 under possible future emission scenarios?

Lead discussants: Jason West, University of North Carolina; Uma Shankar, U.S. EPA

- Radiative forcing (RF) is a perturbation in the net radiative flux at the top of the atmosphere because of a change in a radiatively active forcing agent. The impact of O_3 RF on anthropogenic CO_2 warming varies across different regions of the planet. Climate variables such as precipitation and temperature, as well as atmospheric circulation patterns, can have regional impacts.
- Uncertainties exist in model estimates of the spatial distribution of RF and temperature changes. The AR5 reported a medium confidence in the RF estimates from 1850 to 2000 in the Atmospheric Chemistry and Climate Model Intercomparison Project (ACCMIP) because of the large standard deviation among regions. Uncertainty in the O_3 climate impacts is due to confounding climate variables and a lack of supporting literature.
- In IPCC AR6, O_3 RF is estimated at +0.47 [−0.24, +0.70] W m^{-2}, which is 18% higher than reported in IPCC AR5. The revised estimate is based on a better understanding of the distribution of present-day tropospheric O_3, and limited available constraints on pre-industrial O_3 through isotopic analysis of ice cores.
- The CASAC review of the previous O_3 ISA pointed out that there is a clear causal relationship between O_3 and global mean temperature, which leads to a small (0.1°C–0.3°C increase from pre-industrial values) but significant contribution to climate warming. IPCC AR6 studies report a slightly greater degree of warming (0.37°C) during the 1850–2013 period. However, the effects of O_3 on other climate change indicators (e.g., changes in atmospheric circulations evidenced by changes in weather and precipitation patterns) are not clear because of a lack of agreement among models and a lack of study data. A current challenge in modeling studies is connecting regional-scale O_3 concentrations to regional-scale RF and warming. Isolating the O_3 climate influence in the United States is complicated because of (a) emissions of O_3 precursors from outside the United States (e.g., Southeast Asia), and (b) the confounding impact of other short-lived climate forcers (SLCFs).
- It is important to study the effects of tropospheric O_3 on ecosystems and their feedback to climate via changes in the terrestrial carbon sink. Carbon sequestration by the land surface was an endpoint evaluated in the 2020 ISA as likely to have a causal relationship to O_3 via its adverse

impact on vegetation. Changes in NO_X concentrations also affect vegetation. The net impacts of these changes are hard to quantify because of variability among species and their spatial distributions. The IPCC AR6 demonstrates the link between CO_2 and O_3, but the degree is still unknown.

- Controlling one air pollutant may exacerbate others, creating a challenge for regulation. In this context, the role of methane in reducing tropospheric O_3 is important for both climate and health endpoints. While NO_X emissions reductions are traditionally used to improve O_3 air quality, they result in increasing the lifetime and atmospheric concentration of methane and are therefore a climate penalty. Reductions in VOCs and CO, on the other hand, avoid this penalty and offer a better approach to simultaneously reducing O_3 climate impacts and mitigating other welfare and health impacts. Examining the impacts of O_3 precursors—methane, NO_X, VOCs and CO—more holistically can provide more useful information on the impacts of O_3 than attempting to isolate an effect that would require expensive and time-consuming climate model simulations to obtain a statistically robust signal.

Question-and-Answer Session

What is the current understanding about the large range of soil NO_X emissions values in the scientific literature?

- Satellite data can be used to understand the range of values, especially in rural areas with little previous monitoring.
- Soil NO_X emissions occur after fertilizer application, which has been an understudied area.
- It is hoped that increases in observation density in these areas will improve understanding of soil NO_X emissions.
- Models generally agree that reductions in NO_X will cause a methane increase and an O_3 decrease, although reducing VOCs will free up some hydroxyl radicals, which could address methane.
- Models have regional differences, but emissions of CO have the same effect across regions, regardless of the emission location.
- For VOCs, models often have varying simplistic representations of secondary organic aerosols, contributing to the spread across models.
- Answering the question on soil NO_X solely with satellite data is challenging because of the amount of unconstrained spatial and temporal variability.
- Different models have very different estimates for soil NO_X emissions, due in part to regional differences in soil and microbes.

Can O_3's causal impact on temperature be accounted for in contributions to wildfires and can it be subtracted from background?

- Wildfires are governed by many things in addition to temperature. Although it would be novel to investigate the impact of temperature alone, it would likely be a small contribution compared with those of precipitation and soil moisture. Many of the factors depend on wind and soil moisture and changes in these factors may be due to climate changes. Teasing out the impact of a single pollutant on the climate is difficult.
- Even if some of these factors could be modeled correctly, translating them into a standard

would be long and difficult. It may be better to look at a subset of our understanding to develop standards instead.

How can tropospheric mixing be quantified?

- Some stratospheric-tropospheric exchange processes are two-way, but usually it is just the mixing of lower concentrations with higher concentrations. It would be challenging, but possible, to quantify this process with other tracers.

Tuesday, May 14, 2024

Session 1: Planning for the Review of the Welfare Effects Evidence and Analyses: Review of Welfare Effects Evidence

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Jeffrey Herrick, U.S. EPA; Kris Novak, U.S. EPA; Emmi Felker-Quinn, National Park Service

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. The co-chairs noted that the CAA definition of the effects on welfare includes, but is not limited to, effects on soils, crops, vegetation, animals, wildlife, and climate. The presentation covered the scope of ecological evidence considered in the ISAs and an overview of causality determinations from the 2020 ISA.

Topic 1: Ecosystem Processes

Discussion Question:

What new information is available about O_3 effects on ecosystem processes, such as water cycling, carbon sequestration, productivity, and belowground/biogeochemical cycling?

Lead discussants: Danica Lombardozzi, Colorado State University; Doug Kaylor U.S. EPA

Question panelists: Lisa Emberson, Emmi Felker-Quinn, Jason Lynch, Jeffrey Herrick

- The effects of O_3 on water cycling continue to be complex, occurring at multiple scales ranging from altered stomatal response and water use in plants through measurements and models of ecosystem water use. One approach to the topic may be to use plant water-use efficiency as an integrated measure that can be related to transpiration; water cycling; carbon assimilation, allocation, and sequestration; biomass; and yield. Another approach might be looking at measurements of plant stress, of which water or drought stress is a part, which could incorporate larger spatial scales and remotely sensed data.
- Experts highlighted that many current studies do not examine O_3 effects in isolation, but as a suite of other factors, and that multifactorial designs should be assessed in the ISA.
- A few of the studies mentioned linked CO_2 and O_3 effects on terrestrial carbon and nitrogen cycles. There is research examining O_3-related impacts to nitrogen cycling via changes in bacterial and fungal communities. Additionally, a recent meta-analysis assesses how belowground functions respond to elevated O_3 concentrations.
- Experts agreed that models, particularly process-based models, might be important when scaling from leaf to canopy level to estimate O_3 effects on water cycling, carbon assimilation, and carbon and nitrogen allocation. This approach is, however, a future avenue of research, and the current state of modeling is not capable of estimating ecosystem level effects from O_3 exposures.
- The importance of considering both short- and long-term effects was highlighted.
- Because there are different diurnal patterns of exposure and different bioregional factors (climate, soil type, plant functional type, water dynamics), as well as species-specific stomatal disfunction, it is important to think about individual ecosystem types and not apply models or functions across ecosystems without regard to these differences.

Topic 2: Community-level Effects

Discussion Questions:

Question 1: What new information is available about O_3 effects at the community level such as biodiversity, community composition, and species interactions?

Question 2: What new information is available on O_3 effects on volatile plant signaling compounds and plant-insect signaling?

Lead discussants: Emmi Felker-Quinn, National Park Service; Meredith Lassiter, U.S. EPA

Question panelists: Lisa Emberson, Doug Kaylor

- O_3 alters aboveground ecological communities (conifer forests, broadleaf forests, grasslands, agricultural systems—specifically interactions between crop species and weed species growing in the same place, agroforestry) by decreasing the abundance of sensitive species and giving tolerant species a competitive advantage. Information available since the release of the 2020 ISA supports these findings. Effects are also reported in lichens and in the endosphere and phyllosphere (biome of micro-organisms living on and inside plants).
- The belowground soil microbial community (including mycorrhizae, bacteria, and archaea) and soil invertebrate community composition shifts are likely due to cascading effects of O_3 on plant chemistry and plant carbon allocation to leaves, wood, and roots. Many of these experimental studies include one or more modifying factors (i.e., CO_2, nitrogen, warming, precipitation). Emerging topics in microbial community effects since the 2020 ISA include ecosystem multifunctionality and network stability.
- Plant and microbial community responses in grasslands were highlighted as an example of the complex interactions between aboveground and belowground communities under elevated O_3. Although much of this literature is from the previous decade, studies further examine belowground interactions and additional factors that modulate O_3 effects. For example, grasslands with lower nitrogen deposition have a greater response to O_3 stress than those with higher nitrogen deposition, indicating stress history as a factor in O_3 response.
- Effects of O_3 on biogenic volatile organic compounds (BVOCs), which plants emit to signal to other community members and potential pollinators, were an emerging area of research during the development of the 2020 ISA. Approximately 50 studies are now available on BVOCs, primarily focused on pollination, with several studies on herbivore-plant and plant-plant signaling.
- O_3 impacts plant-pollinator interactions in three ways: 1) direct alteration of plant physiology affecting the quantity and quality of BVOCs, 2) alteration of chemical signals in the air column through reactions with O_3, and 3) detection and perception of scents by pollinators. Recent studies further characterize each of these areas or report new endpoints, such as monitoring of pollinator antennal responses to floral blends. Other recent signaling studies have focused on the potential link between pollinator behavior, O_3 exposure, and plant yield, which includes examining the number of visits to plants from pollinators and the abundance of pollinators in fields.

Topic 3: Population/Individual Level Effects

Discussion Questions:

Question 1: What new information is available about O_3 effects at the population or individual level, such as survival, growth, reproduction, phenology, visible foliar injury, and crop yield?

Question 2: In particular, is there new information on non-tree species, non-commodity crops, and species that are threatened and endangered or culturally significant?

Question 3: What new information is available on O_3 effects on insect herbivores and other wildlife?

Lead discussants: Ripley Tisdale, USDA; Jean-Jacques Dubois, U.S. EPA

Question panelists: Jason Lynch, Doug Kaylor, Meredith Lassiter, Susan Sachs, Amy Luo

- The panelists reviewed and discussed National Park Service (NPS) community science data collection efforts in Great Smoky Mountains National Park. Data collection on O_3 injury to two species of an herbaceous perennial has been ongoing since 2003. One of those species, *Rudbeckia laciniata*, is culturally important to Native American groups. Panelists discussed the variation in the severity of injury observed over the period of data collection, and the interacting weather variables that might have modified it. Of particular interest to the panelists was the possibility that since 2003, measured O_3 concentrations have decreased overall in the study area, whereas injury may have increased. Specifically, observations of injury occurred while O_3 concentration was below 100 ppb. The Kohut et al. 2012 article was referenced and potential upcoming publications were discussed, as were recent updates to the NPS list of O_3 bioindicator species.
- The panel noted that the COVID pandemic may have provided opportunities for natural experiments on the effects of O_3 exposure on crop yield. During the initial pandemic lockdown, annual European and global emissions dropped significantly by 30% –50%, and yield improved by 2%–8%. In the United States, the soybean yields only recovered approximately 0.02% during the COVID lockdowns in 2020. Potential interacting factors were discussed.
- Other topics briefly mentioned were research on effects of nitrogen fertilization, crops on which impacts of O_3 have been reported, and effects on belowground plant parts. Modeling efforts were also briefly discussed, with special attention given to the importance of exposure metrics.
- Recent studies on the effects of O_3 on vertebrates were reviewed briefly. One study of effects on fruit fly hybridization was also referenced.
- Further discussion of the impacts of O_3 on crop yield was deferred to the next discussion session.

Topic 4: Exposure/Dose Response

Discussion Questions:

Question 1: What new information is available on linking concentration weighted metrics (e.g., W126 and AOT40) to response of species found in the United States?

Question 2: Is there new information linking flux metrics to effects on species that occur in the U.S.?

Lead discussants: Lisa Emberson, University of York; Jeffrey Herrick, U.S. EPA

Question panelists: Emmi Felker-Quinn, Olivia Clifton, Jean-Jacques Dubois, Huiting Mao

- The panelists discussed the cumulative concentration weighted metrics (e.g., W126 and AOT40) for measuring exposure that are currently being used in the United States and in some cases in Europe. The bases of these metrics were discussed in the context of available data on plant species in the United States. The main paper discussed was Lee et al. (2022), which reported W126 response functions in 16 U.S. tree seedlings. In another study, Li et al. (2023) linked the AOT40 metric to effects on C3 and C4 crops that are grown in the United States.

- Cumulative concentration weighted metrics were discussed as NPS's W126 benchmarks to protect vegetation. In the NPS, 7 ppm-hrs W126 and 13 ppm-hrs W126 benchmarks are used for tree seedling biomass loss. It was noted that O_3 is estimated by interpolation in parks using these benchmarks.
- The panel discussed flux-based metrics and pros and cons of the European methods of flux. The 2023 update of the *Manual on Methodologies and Criteria for Modelling and Mapping Critical Loads and Levels and Air Pollution Effects, Risks, and Trends* provides more information. This update included four crops (wheat, potato, tomato, and rice), five forest trees (beech, birch poplar, Norway spruce, Mediterranean deciduous oak, and Mediterranean evergreen), and one grassland crop (perennial ryegrass). The phytotoxic O_3 dose (POD) was discussed, which has advantages as a more biologically meaningful descriptor of O_3 exposure and incorporates the influence of abiotic stress, such as heat or water stress, when compared with AOT40. However, there are challenges with the amount of data required to calculate POD. Several studies were discussed that explored the question of calculating flux metrics, including Braun et al. (2014), Mills et al. (2011), Pleijel et al. (2022), Nelson et al. (2018), and Peng et al. (2019).
- Researchers on the panel discussed studies calculating flux metrics and POD on vegetation in the United States. However, it was noted that there are very few measurements linking effects on plants to calculated flux metrics in the United States. Linking O_3 flux to effects on U.S. vegetation is an important area of future research. Some of the studies discussed on estimating O_3 flux in the United States included Anav et al. (2022), Clifton et al. (2020), and Mao et al. (2024).

Topic 5: Climate and Other Modifying Factors

Discussion Question:

Question 1: Is there new information on how O_3 affects ecosystems and how its components are modified by climate change and other factors (e.g., temperature, soil moisture, nutrients, and/or other pollutants)?

Lead discussants: Jason Lynch, U.S. EPA; Kris Novak U.S. EPA

Question panelists: Emmi Felker-Quinn, Doug Kaylor, Danica Lombardozzi

- Previous NAAQS reviews have shown that nitrogen deposition, CO_2, and climate variables may exacerbate or negate the effects of O_3 on plants. Recent studies were discussed that have reported on the modifying factors of drought and excess nitrogen (Grulke and Heath 2019; Out-Larbi et al., 2020), CO_2 (Tai et al., 2021; Watanabe et al., 2022), nitrogen (Feng et al., 2019; Watanabe et al., 2022; Li et al., 2020), and temperature with O_3 (Lee et al., 2020).
- The issue of excess nitrogen across the United States was emphasized and continues to be a stressor in ecosystems. While oxidized nitrogen has decreased in many areas, ammonia, on the other hand, has increased. The form of nitrogen can have varying effects on the growth of plants in combination with O_3 exposure and should be considered.
- Panelists highlighted two recent studies reviewing the impact of nitrogen deposition and O_3 that look at root biomass responses (Ping et al., 2020; Fenn et al., 2020). It was also noted that nitrogen deposition can affect plants not only through increased soil nitrogen, but also via foliar uptake of nitrogen, which should be considered as we aim to understand the role of O_3 uptake, because they use similar pathways. The load of nitrogen deposition is also important when considering whether it will have a beneficial or deleterious effect.
- Available datasets (derived from Forest Inventory and Analysis measurements) of mature tree

growth and survival exposure-response relationships with W126 O_3 exposure were discussed and can possibly be tested and modified with temperature and precipitation projections.

- The panel mentioned a recent meta-analysis by Shang et al. 2024 discussing the impacts of drought and O_3 on the different parameters related to quantifying photosynthesis, which could be very useful for consideration in future modeling.
- Both drought and temperature should be considered, especially because temperature and O_3 increase together. Concurrent changes in humidity can also affect stomatal functioning and should be included in studies exploring the effects of O_3.
- Previous research and theories suggest that elevated CO_2 may result in stomatal closure and subsequent reduced water loss and increased water-use efficiency. From an ecosystem perspective, CO_2 may also increase leaf area indices, which increases tree water loss rather than reducing it, underscoring the need for more whole-plant/ecosystem approaches to assessing these interactions.
- A recent study by Ainsworth et al. (2020) suggests that "the terrestrial biosphere is currently at a turning point shifting from a period where carbon dioxide and nitrogen fertilization dominate the global carbon cycle to a period when warming and drought stress dominate."
- The panelists agreed that O_3 needs to be considered as a suite of complicated multivariate stressors on plants, together with drought, climate, humidity, and other factors.

Question-and-Answer Session

Are there any studies on O_3 impacts to wetland species in riparian zones, where soil moisture conditions are variable?

- The panelists recalled there may be studies from the 1990s and 2000s on this topic. A study was noted by Kohut et al. (2012) in Rocky Mountain National Park where cutleaf coneflower displayed more visible O_3 foliar injury in riparian areas.

Do researchers find effects from mycorrhizal associations, we find that the effect of CO_2 fertilization on plant growth is contingent on complex interactions between N availability and mycorrhizal association. Is there a similar interaction with O_3?

- The panelists were unaware of any studies that directly examine this association. However, this topic was covered in the community belowground section of the 2020 ISA.

With all of these methods of calculating flux on the landscape level, how do we do that for the United States and is it possible to link it to actual effects? What would be the best way to approach the issue?

- The panelists suggested obtaining as much data as possible for calculations and future studies will have a range of estimates for O_3 flux/deposition to contribute to the understanding of this topic.

Session 2: Welfare Risk and Exposure Assessment

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Leigh Meyer, U.S. EPA; Kris Novak, U.S. EPA

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They provided the history of the O_3 NAAQS, the current secondary O_3 standard, the currently available welfare evidence and associated uncertainties, and the general approach for planning the upcoming risk and exposure analyses.

Topic 1: Modeling O_3 Gradients

Discussion Questions:

Question 1: O_3 concentration gradients exist across the United States and are influenced by the location of emission sources and O_3 chemistry and transport. Reflecting those concentration gradients can be important in understanding the protection provided by the O_3 standard. What modeling approaches are available and might be employed to estimate ambient air O_3 concentrations across large areas, including forested areas and the sources that influence air quality in these areas? What is an appropriate approach to model or estimate O_3 impacts upwind of urban areas?

- How might this be done to simulate different air quality scenarios, including one for when the design value is just meeting the current standard?
- What kind of case study areas or parts of the United States might be appropriate to include in this assessment?

Lead discussants: Ben Wells, U.S. EPA; Barron Henderson, U.S. EPA; Olivia Clifton, NASA; William Vizuete, University of North Carolina

- The discussion highlighted the difficulties in modeling and computing capabilities for predicting how observed O_3 responds to hypothetical emissions by adjusting concentrations using modeled sensitivities.
- The EPA Air Quality Assessment Division stated its intent to investigate modeling and computing capabilities to assess the possibility of modeling multiple years and emissions levels and reflected on the challenges of the models, such as computational constraints and modeling bias, which was large enough that data fusion would have been unstable. Alternative modeling methods or tools that could be applied on an hourly basis and then aggregated will be investigated.
- The panel deliberated the strengths and weaknesses of different model types, possible corrections, and the use of artificial intelligence (AI) tools to improve model performance and computational efficiency.

Topic 2: Climate Change Risk and Exposure Assessments

Question 1: How might climate change (e.g., temperature, precipitation changes) be reflected in the air quality scenarios included in the risk and exposure assessment? Are there climate change policies that should be accounted for in the assessment? What analytical approaches could be used to assess the influence of current climate change on risks to vegetation?

Lead Discussants: Rachel Sales, U.S. EPA; Drew Shindell, Duke University

- The discussion highlighted the uncertainties and variability in predicting future climate change, and how this might affect any inclusion of climate change in air quality scenarios. For example, wildfire intensity and frequency are likely to change in the future but there are a lot of uncertainties around predicting wildfires.
- Another point of discussion was how climate change might affect seasonality, which in turn might affect O_3 measurements.
- Panelists also discussed international climate change and O_3 policy, particularly the importance of methane policies, and how policies targeting methane might be salient in the future.
- Finally, the panelists and discussants deliberated the strengths and weaknesses of longer versus shorter time scales, and how shorter time scales and simpler models might be a path forward

for including climate change impacts in future O_3 reviews.

Topic 3: Exposure-Response Functions

Question 1: Recognizing the important role that species-specific exposure-response functions have played in past reviews, are there new data or information that should be incorporated to improve our understanding of these data and resulting exposure-response functions? Are there different analytical approaches that should be utilized?

- Are there other approaches that should be considered, including approaches that might incorporate metrics for both peak concentrations and for cumulative/sustained exposures on tree seedling biomass?
- How can the dataset be analyzed differently to provide a clearer understanding of the patterns of ambient air O_3 concentrations common today (e.g., reduced prevalence of peak concentrations)?

Lead Discussants: Travis Smith, U.S. EPA; Lisa Emberson, University of York

- Panelists discussed the strengths and weaknesses of various O_3 metrics, such as the AOT40, W126, POD1, and various flux measurements. These measurements could be used in exposure/response functions.
- Panelists noted that previous research using flux metrics focused on European tree species. Lead discussants noted that flux metrics could likely be applied to U.S. tree species, with some adjustments for sensitivity.
- Panelists discussed peak and chronic exposure to O_3, uncertainties in how exposure-response relationships might change over a tree's lifetime (i.e., mature versus seedling), and how critical loads might be incorporated into exposure/responses functions.
- The discussion concluded with discourse over future directions. Panelists thought that various metrics should be considered in this review and that crop exposure/risk models should be incorporated.

Topic 4: Community Forest Impacts

Question 1: What approaches and methods are available to estimate O_3 tree community forest impacts (e.g., species diversity and richness) considering interspecies competition and other interactions? For example, what are current methods for modeling O_3 concentration scenarios against tree species competition over a period of time? What are their strengths and limitations?

- Are studies, methods, or approaches available that might be used to relate extent and magnitude of foliar injury in forested areas to public uses/values and ecosystem services that might inform judgments of public welfare significance?

Lead Discussants: Kris Novak, U.S. EPA; Emmi Felker-Quinn, National Park Service

- The discussion highlighted how species-specific responses to O_3 could be applied to other species and potentially scaled up to inform community changes. Panelists noted that the environmental conditions also affect species-specific responses.
- Panelists and lead discussants discussed the importance of visible foliar injury to public welfare. Discussants noted that visible foliar injury can be used to inform the public about less visible air quality measurements.
- The discussion concluded with a deliberation of plants with high cultural value, and the

sensitivity of such plants to O_3. Panelists noted that Tribal input on culturally important plant sensitivity to O_3 would be valuable in upcoming reviews. It was noted that O_3 exposure can also degrade the nutritional value of certain plants, which can degrade cultural resources. Discussants recommended that O_3 effects on plants of cultural value be considered in future reviews.

Question-and-Answer Session

- The question-and-answer session considered different models and modeling techniques for stand dynamics, tree growth and survival, forest structure, and competitive dynamics.
- Discussion also included how a range of metrics may be used in the risk and exposure analysis and linked to various air quality scenarios.

Does the discrepancy between the policy need for an ambient metric in contrast to the flux-based approach used in recent science make the W126 more feasible compared with a flux metric?

- The standard needs to be an ambient metric.

Can an ambient metric be used for the NAAQS, while a range of metrics could be used for risk assessment to understand the implications of the NAAQS and interpret the meaning of exceedances?

- This option is possible. Combinations could be used in tandem, and perhaps flux could be assessed there.
- For assessment purposes, focus is placed on what is scientifically appropriate and feasible in terms of tools and data for analyses. Risk estimates can be linked to air quality scenarios, which are characterized based on various metrics, and those inform how the standard is characterized. The assessments should rely on an appropriate metric (referencing the use of the W126 metric in the 2015 Air Quality Assessment as an example).

Wednesday, May 15, 2024

Session 1: Human Exposure to Ambient O_3

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Peter Byrley, U.S. EPA; Michael Jerrett, UCLA

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They noted that O_3 exposure was defined in the last ISA as the interface of the breathing zone with a particular concentration of a specific pollutant over a certain period of time. O_3 can be monitored in various ways, including the use of fixed-site and/or personal monitors. For modeling, many models are available including proximity-based models, spatiotemporal models, mechanistic models such as chemical transport models, more complex hybrid models that incorporate multiple types of data, and models that use newer machine learning methods. In the last review, one of the conclusions was that there were more studies that utilized chemical transport modeling for O_3. They highlighted the need to include spatiotemporal considerations such as local traffic that emit O_3 precursors. Errors are often similar over urban scales because ambient O_3 concentrations tend to have low spatial variability. The co-chairs also discussed potential sources of exposure error that may impact epidemiologic outcomes and presented information on potential confounding present in O_3 measurement.

Topic 1: Exposure Surrogates, Errors, and Measurement/Modeling Approaches

Discussion Questions:

Question 1: What new information is available on the relationship between ambient O_3 concentrations and personal exposures in various microenvironments, including infiltration from outdoor to indoor environments?

Question 2: What new information is available to improve our understanding of the discrepancies between stationary monitor measurements and actual pollutant exposures?

Question 3: What recent advances have been made in monitoring and modeling (including hybrid models that utilize data from satellites, land use information, ground-based monitors, etc.) ambient concentrations of O_3 across locations (e.g., urban vs. rural, monitored vs. unmonitored) to improve understanding of human exposures?

Question 4: How have these approaches been evaluated and validated in various types of locations (e.g., urban vs. rural, monitored vs. unmonitored)?

Lead Discussants: Michael Jerrett, UCLA; Lisa Baxter, U.S. EPA

This discussion highlighted the complexities of the relationship between ambient O_3 and personal exposure and included discussion of emerging measurement and modeling techniques being used to improve the understanding of this relationship. Several points were raised:

- The use of satellite data and ensemble models has improved the ability to estimate ambient O_3 concentrations, but personal exposure remains challenging to measure accurately. GPS tracking has been developed to account for time-activity data, such as, but these have not penetrated epidemiology as a discipline.
- Indoor O_3 levels are significantly lower than outdoor levels because of the indoor reactivity of O_3, ventilation, and the scarcity of O_3 sources indoors.
- Fine-scale spatial data are lacking for O_3 but are necessary for accurate exposure assessment. High-density monitoring and personal monitoring data are needed to better understand these

relationships.

- Outdoor activities, such as exercise, can modify the health effects of O_3. Climate change and extreme weather events also affect O_3 exposure.
- Climate change and seasonality of O_3 need to be better understood. Trends such as ventilation, increasing air conditioning usage, and wildfires may change the understanding of seasonal O_3 exposure.
- Multipollutant analysis (including NO_X and VOCs) at fine scales would aid in understanding O_3 chemistry and exposure.

Topic 2: Exposure to O_3 in a Multipollutant Environment

Discussion Questions:

What new information from measurement and modeling approaches is available to characterize the relationships between O_3 exposures and exposures to other ambient air pollutants? Does this new information provide insight into the potential for co-pollutants confounding health studies?

Lead Discussants: Jeffrey Brook, University of Toronto; Peter Byrley, U.S. EPA

The discussion highlighted the complex interactions between different air pollutants, the need for a more comprehensive approach that considers total oxidant exposure, and assessment of the health impacts of photochemical oxidants in urban environments. Several points were raised:

- O_3 can interact with complex urban air mixtures, forming an array of pollutants that may have varying health effects across different locations.
- There is a need to consider total oxidant exposure, rather than relying solely on O_3 measurements, to better understand and assess the health impacts of these complex air pollutant mixtures.
- Expanding monitoring efforts to include a broader range of oxidants and pollutants could help explain variations and discrepancies in current data and provide a more comprehensive understanding of the health effects associated with these mixtures.
- Epidemiologic studies have shown that the chronic health effects of $PM_{2.5}$ are enhanced in the presence of oxidant gases like O_3.
- Statistical methods that can analyze the independent and combined effects of multiple pollutants could be useful in informing the ISA and addressing environmental justice concerns in urban communities.
- While the current approach focuses on O_3 alone, more research is needed to understand the health problems experienced due to the complex interactions between various air pollutants in urban environments.

Question-and-Answer Session

How will the enhanced exposure estimates, which are not uniform across pollutants, impact our understanding of O_3 health effects in multipollutant epidemiologic studies, and what new challenge associated with relative improvements in exposure estimates has been introduced in interpreting the roles of respective pollutants and health outcomes?

- There is concern about the ability to develop the best NO_2 model and the best O_3 model and combine them in an analysis. These models may need to be codeveloped to understand the nature of the chemical mixtures in the atmosphere.

- Previous simulation studies have demonstrated that when looking at two pollutants, the one measured with more precision might dominate the statistical modeling, and because of this, multipollutant results must be interpreted carefully. Interpreting these complex and multivariable analyses may be an area that machine learning could help.

O_3 and NO_2 are positively correlated in some environments and negatively correlated in other environments. How would you expect this varying relationship to affect results of epidemiologic studies looking at O_3 that include NO_2 as a potential confounder?

- Not all NO_2 is the same and therefore may interact in both the environment and with human health in varying ways. Some NO_2 may be more correlated with O_3 but interact very differently in environments with various mixtures.
- Various monitoring mechanisms are available for indicators for total photochemical oxidants, which may be an approach for collecting data.
- Current work is investigating how control strategies may change as a function of space and time across a place with heterogenous emission inventory.
- Sources could give some insight on oxidant potential. Measuring O_3 is becoming more complex because long-haul transportation emissions from other countries impact U.S. measurements.
- Other chemical mixtures that may interact with O_3 and other oxidants would be feasible to monitor. More information on the effects of exposure to multiple chemicals is something to investigate.

Session 2: Planning for the Review of Health Effects Evidence: Emerging Evidence and Interpretation

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: David Lehmann, U.S. EPA; Howard Chang, Emory University

Session cochairs provided an overview of the ISA process for reviewing health evidence related to O_3 exposure. They detailed its multi-step approach, which includes literature searches, screening, quality evaluation, and the integration of evidence from epidemiologic, animal toxicological, and human studies. The cochairs also briefly reviewed the causality determinations made in the 2020 ISA, which issued 13 causality determinations for seven major health outcomes. A five-level hierarchy was employed to classify the weight of evidence: short-term respiratory effects were deemed "causal," while long-term respiratory effects and short-term metabolic effects were considered "likely to be causal." Most other outcomes were categorized as "suggestive" of causality. Additionally, the session cochairs introduced the aims of the session and key discussion questions. These questions focused on identifying emerging evidence for new and previously reviewed health effects, assessing biological plausibility, exploring methodologies to evaluate effect modifiers and exposure patterns, and examining studies from diverse geographic regions. Finally, the session cochairs introduced lead discussants and the panelists.

Topic 1: Emerging Evidence, Health Outcomes, and Methods

Discussion Questions:

Question 1: The last O_3 ISA evaluated evidence for respiratory effects, cardiovascular effects, metabolic-related health outcomes, reproductive and developmental outcomes, nervous system effects, cancer, and mortality. Since the last review, what new or emerging O_3-related health effect endpoints have been evaluated in epidemiologic, controlled human exposure, or animal toxicological studies (e.g., cognitive decline, autism, immune effects)?

Is there new evidence that further informs endpoints included in the 2020 ISA? Specifically, is there new evidence that 1) is consistent with causality determinations in the 2020 ISA; 2) contradicts causality determinations in the 2020 ISA; or 3) further improves the understanding of biological plausibility, health outcomes for at-risk populations, and health outcomes at lower O_3 concentrations?

Lead discussants: Parker Duffney, U.S. EPA; Alex Carll, University of Louisville

- Emerging research areas/findings include neurodegenerative diseases, cognitive decline, autism spectrum disorder, out-of-hospital cardiovascular effects and arrythmias, kidney and liver disease, and the impact of COVID. Also, the role of the hypothalamic-pituitary-adrenal (HPA) axis in O_3-induced effects is becoming more well studied.
- There has been a proliferation of epidemiology studies and chronic obstructive pulmonary disease (COPD) and interstitial lung disease studies.
- There is more attention in the literature to the interaction of O_3 with temperature and climate on health outcomes.
- It was pointed out that what constitutes low O_3 concentration should be reconsidered.
- The EPA was advised to be sure to include nasal effects, which include nasal scrubbing of O_3 impacting exposure in the lower airways as well as health effects relevant to the nose, such as allergic rhinitis and the ability of O_3 to act as an adjuvant to subsequent challenge.
- The need to account for impact of outdoor activity on outcomes like metabolic disease was stressed. When considering controlled human exposure studies, the EPA was reminded to keep in mind that morbidity-related endpoints may be missed with the use of predominantly young healthy individuals in controlled human exposure studies.
- The importance of developing a better idea of true exposure from ambient air was raised. The point was made that one's overall exposure is related to both indoor and outdoor O_3 exposure and that indoor penetrance of O_3 is much less than other NAAQS pollutants, like particulate matter.
- There is growing interest in the role of BMI on health responses to O_3, although this has not been well studied in controlled human exposures. This is potentially relevant to endpoints related to lipid profile changes.
- Finally, the EPA was advised to think forward about how to interpret and apply data derived from new experimental approaches like 'omics' and single cell investigations.

Question 2: Have recent controlled human exposure or animal toxicological studies examined the potential mechanisms of action by which short-term and/or long-term O_3 exposures may result in health effects, particularly cardiovascular effects and other effects not determined to be "causal" in previous ISAs? Do recent experimental studies provide insights into the biological plausibility of these O_3-induced effects?

Lead discussants: Aimen Farraj, U.S. EPA; David Peden, University of North Carolina

- The point that there are responders and nonresponders to O_3 was mentioned, as well as the lack of understanding that drives one's response to O_3. Subset analysis of controlled human exposure data can help to identify subsets particularly at risk.
- Expand exercise, low-level exposure, and lower dose studies to provide the most useful

information to the community.

- There is a need to expand the controlled human exposure endpoints to those outside of the lung/respiratory system to help provide additional information about health effects seen in epidemiologic and animal studies.
- EPA was advised to think about how to apply other indicators of effects and new data types (e.g., "omics") and revisit older datasets to apply current approaches to analyzing data when possible.
- Noting that the controlled human exposure evidence was inconsistent, downgrading the causality determination from "likely" to "suggestive of causal relationship" was brought up. It was pointed out that we do not really understand the origins of the variability. The point that we are not all the same was stressed, even when focusing on healthy populations.
- Very few mechanistic studies have been published since 2020, except for some work by Urmila Kodavanti.

Question 3: What new or emerging methodologies or study designs are available in epidemiology to (1) address potential effect modifiers (e.g., genetic traits and socioeconomic status) and confounders (both chemical and nonchemical stressors); (2) disentangle the effects of long-term exposure and short-term exposure to O_3; (3) better understand potential heterogeneity in O_3 effects assessed in U.S. multicity studies; and (4) understand the role of O_3 as a mediator?

Lead discussants: Howard Chang, Emory University; Kristen Rappazzo, U.S. EPA

- There are no new techniques for effect modifiers, but there are some emerging methods in the statistics literature that require additional development before application to effect modifiers.
- It was noted that although there are no major new techniques, there is an increased appreciation for accounting for a core set of modifiers in all studies, including temperature and climate. Techniques using machine learning are still early in development.
- While techniques for addressing confounders in other fields are available, they do not seem to have been applied to O_3 thus far. Causal methods have been applied to this type of research, but the point was made that potential confounding factors were not always included in the models.
- Not many studies look at both long- and short-term exposure to O_3 because it is inherently very difficult to study both simultaneously. Some advancements have been made, however, related to identifying sensitive windows during development.
- No new methods have been developed for addressing heterogeneity.
- There are a few papers on how O_3 can act as a mediator for temperature effects.

Topic 2: Interpretation of Evidence

Discussion Questions:

Question 1: What factors are important to consider when evaluating epidemiologic studies conducted in geographic regions less representative of conditions in the U.S. (e.g., in terms of sources, air quality mixtures, exposure patterns, population characteristics)?

Lead Discussants: Lisa Baxter, U.S. EPA; Antonella Zanobetti, Harvard University

- Even within the United States there is significant variability in, for example, air quality.
- Precursors vary across the United States. When interpreting results, it is important to think

about potential differences in the application of findings in a regulatory context.

- It might be useful to compare results from different regions across the country. In this way, the EPA may better understand the potential health impact of variability in conditions in different regions.
- Some studies look at rural versus urban; the EPA could assess whether these comparisons have been captured in previous ISAs.
- Studies looking at mortality are conducted in cities, while many people reside in nonurban areas where conditions are different.
- Newer epidemiologic studies have been conducted in Asia and Europe, although not about O_3 specifically. One panelist recommended that the EPA reviews/considers these studies because they have the potential to be relevant to U.S. populations, provided they were properly conducted and report enough information to make meaningful comparisons across geographies.

Question 2: To what extent is new scientific evidence becoming available from experimental or epidemiologic studies to improve the understanding of effects associated with various patterns of O_3 exposure (e.g., repeated short-term exposures to “peak” concentrations versus longer-term exposures to “average” concentrations)?

Lead Discussants: James Brown U.S. EPA; Kristen Rappazzo, U.S. EPA

- The panelists noted that their responses to earlier questions largely covered this question and, for that reason, there was relatively little discussion among the panelists related to this question.
- The point was made that it is important to utilize different exposure designs when considering patterns of O_3 exposure.

Session 3: Planning for the Review of Health Effects Evidence: Evidence Integration

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Parker Duffney, U.S. EPA; Dave Peden, University of North Carolina

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They introduced the session as a holistic view of the entire evidence base and a consideration of issues in integrating multiple kinds of evidence. They gave an overview of the integration of evidence and shared the strengths and limitations of various kinds of evidence, the criteria for causality determinations (a modification of the Bradford-Hill criteria), and the levels of causality based on the amount of uncertainty in the evidence reviewed.

Discussion Questions:

Question 1: To what extent do recent advances in the O_3 health effects evidence support integration of findings across epidemiology, controlled human exposures, animal toxicology, and dosimetry? What does the new evidence indicate regarding consistency of findings within disciplines (e.g., epidemiology studies of cardiovascular mortality versus morbidity)? To what extent do recent O_3 health effects findings from a particular discipline compensate for data gaps in other disciplines?

Lead discussants: Parker Duffney, U.S. EPA; Michael Jerrett, UCLA

Emerging evidence:

- Experts suggest further examining biological plausibility of O_3-induced health effects, especially for short-term cardiovascular effects.

- Coherence of data among disciplines is increasing as well.

Factors to be aware of during evidence integration:

- Antioxidant status and differences between individuals/disease states or species.
- Similarly, understanding of the differences between different experimental species for measuring the outcome of interest.
- Exposure alignment between experimental animal studies and human studies.

How one discipline can compensate for gaps in another:

- There may be a better way to account for study limitations.
- It is critical to acknowledge study limitations and be transparent.
- Strong epidemiologic data can help identify health effects.
- Controlled human exposure studies at low levels can reflect changes in biology that are consistent with health effects seen in epidemiologic studies.
- For animal studies, it is important to understand species differences when considering comparability of reported endpoints to humans (e.g., rodents breathe through the nose and are nocturnal).
- Looking at all lines of evidence is key; there should be some level of coherence and clear articulation of uncertainties to justify stronger causality determinations.

Question 2: What limitations are present in experimental studies that expose humans or animals to "pure" O_3 rather than to the ambient mix of O_3 and related photochemical oxidants (plus other co-occurring pollutants)? Is there new information available for us to better understand the health effects of photochemical oxidants other than O_3 in ambient air?

Lead discussants: Mehdi Hazari, U.S. EPA; Anne Barkley, U.S. EPA

- There is little new evidence for O_3 effects in a mixture. ISAs consider mixture studies when there is also an O_3-alone exposure group.
- There are no data to suggest vast differences between O_3 and other photochemical oxidants.
- Effects of O_3 can be chemical or biological.
- A better understanding is needed of the climate impact on the makeup of relevant photochemical mixtures.
- Discussion in other sessions included how the relevant mixture of photochemical oxidants can look very different in different places and with different sources of precursors and vary temporally throughout the day.
- The role of O_3 in a mixture may be important; effects on transient receptor potential channels was mentioned. Other photochemical oxidants have longer lifespans, which might make time of exposure important to consider.
- Some of this work has previously been done; therefore, review of older literature may be necessary.
- The EPA may need to consider mixtures that are dominated by one gas/oxidant.

- The importance of interpreting animal studies for what they do say and remembering factors that would limit the relationship to results in humans was noted.

Question 3: In the 2020 O_3 ISA, experimental studies were considered for inclusion if subjects were exposed to O_3 concentrations less than or equal to 2 ppm (animals) or 0.4 ppm (humans). These limits were based on findings that the deposition of O_3 from a 2-hour exposure to 2 ppm O_3 in a resting rat is roughly equivalent to deposition of O_3 resulting from a 2-hour exposure to 0.4 ppm in an exercising human (Hatch et al., 1994). Are there new or other data that can inform the potential human health implications of shorter-term animal studies at higher O_3 concentrations? How can recent animal studies examining O_3 exposures well above ambient concentrations inform human responses near the level of the current standard?

Lead discussants: James Brown, U.S. EPA; Annie Jarabek, U.S. EPA

- It is important to consider the dose delivered to the head region, both when considering obligate nose-breathing animals as well as breathing patterns seen in humans at rest versus exercising.
- O_3-related effects in the nose may be underappreciated.
- Biological plausibility studies in animals may necessitate the use of higher concentrations of O_3 exposure.
- The dose cutoff depends on the endpoint. Panelists suggest looking into animal models for thresholds that may be associated with different outcomes (i.e., Dr. Kodavanti's work showing that insulin sensitivity responses occurred at doses that did not cause lung inflammation). The dose relevant to effects was also dependent on animal strain.
- Response depends on time, species, strain, and dose.
- The discussion of relevant exposure concentration cutoff values focused more on animal studies. There was general input that the human evidence cutoff at 400 ppb was sufficient or could even be brought down to the 200–300 ppb range, again acknowledging that the relevant cutoff might be endpoint specific. For animal studies, there may be justification for leaving the cutoff where it is or expanding to higher concentrations, depending on the endpoint.
- Animal studies can be used to help determine how much of a key event is needed to cause downstream effects.

Question-and-Answer Session

Regarding the studies on the effect of O_3 on glucose and insulin response, does the effect persist with chronic exposure, or is the effect only short term?

- It is a short-term effect; the intolerance goes away. However, animals can become desensitized to O_3 exposure. Given the animal responses, type 2 diabetes should be assessed as well.
- A study in preprint assesses a singular gestational exposure to O_3 that led to elevated blood pressure that persisted through pregnancy. Pregnancy is another susceptible subgroup and prior studies have shown lasting effects of O_3 exposures during pregnancy. In addition, neurological effects may develop at subchronic levels.

Thursday, May 16, 2024

Session 1: Planning for the Review of Health Effects Evidence: Public Health Implications

Session co-chair introduction to topics, discussion questions, and panel

Session co-chairs: Alison Krajewski, U.S. EPA; Jason Sacks, U.S. EPA

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They discussed the importance of public health implications and the important questions to consider when evaluating public health impacts, such as population and life stages, exposure conditions, and severity of effect. The co-chairs noted important terms such as susceptibility and vulnerability and the difference between each and explained EPA's intended approach to use the term "at-risk populations" in the ISA. They described the four-category hierarchy the ISA uses for classification (adequate, suggestive, inadequate, evidence of no effect) and further explained what each category entails. They also discussed concentration response and how these thresholds differ from person to person based on the situation and conditions, which makes it challenging to set standard thresholds.

Topic 1: At-Risk Populations

Discussion Questions:

Question 1: To what extent is new evidence available to inform the understanding of subpopulations that are particularly susceptible to O_3 exposures? How can recent evidence from epidemiologic, controlled human exposure, and animal toxicological studies be used to inform conclusions related to at-risk populations, such as genetic traits that may underlie susceptibility or additional life stages or populations (e.g., those with preexisting diseases such as diabetes) potentially at increased risk of an O_3-related health effect? How can recent health effects evidence in particular populations be integrated with other health information (e.g., mechanistic and biological plausibility information) to better understand the public health impacts of O_3 exposure?

Lead Discussants: Jason Sacks, U.S. EPA; Patrick Kinney, Boston University,

- Those who had COVID and then recovered are likely a new at-risk population. In particular, they may be at increased risk for other comorbidities (such as long COVID), but also may be at risk for response to infection since infections may impact the airway and responsiveness.
- In the toxicological literature, some studies examine housing enrichment.
- In the epidemiologic literature, several studies examine cumulative impacts of at-risk factors through indices like a neighborhood deprivation index and social vulnerability index.
- While indices are helpful and provide meaningful insights on the impacts of at-risk factors, they are indices, meaning they look at combined factors rather than tease apart the independent effects of individual factors.
- There was discussion about the separation of pregnancy and birth outcomes as an at-risk factor, but the pregnancy and birth outcomes are part of the reproductive and developmental health chapter or section, depending on the ISA.
- There were several suggestions for potential research ideas that would be helpful for the ISAs, including the O_3 ISA.
- The use of electronic health records (EHRs) and repeated-measure panel studies was discussed to study O_3-related health for populations with defined stress diseases, anxiety disorder, or cardiovascular disease or dysautonomia.

- Environmental justice/redlining was also discussed in the context of identifying potentially at-risk factors or populations.
- There are differences in spatial/temporal resolution of exposures and stressors.

Question 2: Is there new information that identifies a combination of risk factors that can lead to one or more life stages or populations being at greater risk compared to another? What new experimental and observational studies are available to improve our understanding of critical exposure windows?

Lead Discussants: Kristen Rappazzo, U.S. EPA; Judit Marsillach, University of Washington

- There was some additional discussion about the risk factors, including how COVID may impact future research and considerations.
- There was some discussion about identifying critical windows of exposure.
  - The examples come mostly from the literature on reproduction (e.g., methods/approaches for identifying critical windows of exposure for gestational weeks).
  - Time-series studies also might be helpful in identifying critical windows of exposure.
- In addition to chemical co-exposures, it is important to consider the impact of nonchemical stressors (e.g., temperature).
- The combination of at-risk factors is important to know, like indices, but not all factors are equal and there is no existing way to weight these factors.
- Another at-risk factor that is emerging is weight-management drugs for obesity/BMI. The use of these drugs may change how obesity/BMI are considered in analyses.

Topic 2: Concentration Response

Discussion Questions:

Question 1: How do the results of recent studies inform the shapes of the concentration-response relationships for O_3 and various health outcomes (e.g., mortality, hospital admissions), especially for exposures relevant to O_3 concentrations near the current O_3 NAAQS?

Lead Discussants: Antonella Zanobetti, Harvard University; Lisa Baxter, U.S. EPA

- New evidence is limited regarding concentration-response functions.
- There was discussion on how exposure measurement can lead to error and then affect the associations.
- Some simulation models evaluate exposure models and can compare the measurements and distributions for errors and precision.
- To evaluate exposure models, there could be consideration of application of low-cost sensors to help with area/geographies with limited monitoring or measuring.
- There are also differences in exposure measurement/error in some spatial/temporal models.

Question-and-Answer Session

Can you talk about the O_3 metric used as the basis for a threshold of 25 ppb?

- It was an 8-hour maximum and a short-term analysis with a time series.

Session 2: Planning for the Review of Human Exposure and Health Risk Assessments

Session co-chair introduction to topics, discussion questions and panelists

Session Co-chairs: Mary Hutson, U.S. EPA; Tom Long, U.S. EPA

Session co-chairs introduced the topics, discussion questions, lead discussants, and panelists. They noted that this session would review topics already covered in the workshop but would include a broader range of new research and methods, which would inform EPA's quantitative risk assessments for future NAAQS reviews. Four elements are considered when setting and reviewing standards: the indicator, averaging times, form of standard, and level. In the 2020 review, the key evidence was strongest for respiratory effects according to epidemiology and controlled human exposure studies.

Topic 1: Estimating Ambient Air Concentrations

Discussion Question:

Are there new approaches or improvements to estimating ambient concentrations for input into the exposure modeling and epidemiologic-based risk assessment, including O_3 concentrations representing recent conditions and O_3 concentrations just meeting objectives for each air quality scenario, that may be appropriate to consider in this review? Specifically, is there new scientific evidence that can help refine spatial and temporal estimates of O_3 concentrations and/or inform estimates of changing O_3 concentrations due to emissions reductions?

Lead Discussants: Heather Simon, U.S. EPA; William Vizuete, University of North Carolina; Ben Wells, U.S. EPA

- EPA discussed recent improvements in the modeling of ambient O_3 concentrations to account for changes in seasonal and diel distributions of O_3 concentrations.
- The ongoing challenges of addressing other photochemical oxidant sources (e.g., VOCs) in the air quality models as NO_X decreases were noted.
- There is a need for better understanding of the spatial variations in O_3 concentrations to improve the characterization population exposures including potentially vulnerable communities.
    - Low-cost sensors were discussed, but the regulatory requirements for monitoring network placement are aimed to capture data from locations where O_3 levels are expected to be highest, not specific populations.
    - TEMPO could possibly measure boundary layer O_3, but satellite products are better for long-term averaging, not estimating day-to-day variability.

Topic 2: Estimating Exposure Concentrations

Discussion Question:

Are there new scientific developments related to the major components of exposure modeling, including inputs to the model (e.g., microenvironmental concentrations, human activity patterns, differential exposures to population groups, air exchange rate distributions, and indoor air chemistry) that are appropriate for the EPA to consider in its assessment planning? Especially for the APEX model, is there new scientific evidence available that may be appropriate to consider, such as new approaches or tools for evaluating APEX performance (e.g., sensitivity analysis, field studies)?

Lead Discussants: John Langstaff, U.S. EPA; Alex Carll, University of Louisville; Michael Breen, U.S. EPA

- Data inputs for APEX need improvement, particularly ambient O_3 concentrations at fine spatial resolutions.

- The recent incorporation of detailed school calendars from across the U.S. to the activity diaries (CHAD) will improve APEX model inputs.
- A new TracMyAir App—an individual exposure model that aims to predict real-time personal exposures to PM, O_3, and heat—may improve personal exposure estimates that could potentially be used to support exposure assessment model inputs (e.g., CHAD diaries) and evaluate model outputs.
- The TracMyAir App could also evaluate the impacts of individuals who otherwise cannot participate in controlled exposure studies (e.g., people with respiratory diseases).
- The uncertainties related to modeling at-risk populations were highlighted, particularly the need for more information on modeling activity patterns of at-risk populations, which may not be fully captured (e.g., avoidance behaviors) in the current model inputs.

Topic 3: Lung Function Risk Analysis

Discussion Question:

Is there new information that would lessen uncertainties in the lung function models, particularly uncertainties related to exposure circumstances less well studied in the controlled human exposure experiments (e.g., response to low exposures and with low ventilation rates)? Are there approaches or information regarding inter-individual variability in lung function that would support uncertainty and variability characterization for O_3-attributable lung function risk estimates?

Lead Discussants: Jim Brown, U.S. EPA; Jen Sellers, U.S. EPA; Sonja Sax, Epsilon

- Discussion included the availability of new information to lessen uncertainties in the two lung risk function models (Exposure-Response Model and the McDonnell Stewart Smith Model) employed in the 2015 and 2020 reviews and, in particular, uncertainties related to exposure circumstances less well studied in controlled human exposure experiments.
- Issues related to health effects in response to O_3 exposure were discussed, including characterization of adverse health effects, the inter-individual variability of responses documented in the controlled human exposure data, and the impact of prior exposures on the responses.

Topic 4: Exposure to Benchmark Analyses

Discussion Question:

Is there new scientific evidence (e.g., human exposure studies, panel studies) that EPA should consider that could inform benchmark O_3 concentrations, exposure duration, and/or at-risk populations evaluated in the population exposure to benchmark comparison analysis?

Lead Discussants: John Langstaff, U.S. EPA; Dave Peden, University of North Carolina; Sonja Sax, Epsilon

- A recent 6.6-hour controlled human exposure study of 14 subjects at rest (Hernandez et al., 2021) that showed a small but significant decrease in lung function was discussed, along with potential for this study to inform the various exposure and risk models, which included data from studies of similar duration but with exercise.
- There is a need for more at-rest controlled human exposure studies at various durations with more study subjects, including at-risk populations (e.g., people with asthma).

Topic 5: Air Quality Epidemiologic-Based Assessment

Discussion Questions:

Question 1: Do new studies exist that would permit EPA to estimate risks for specific at-risk populations?

Lead Discussants: Neal Fann, U.S. EPA; Michael Jerrett, UCLA; Howard Chang, Emory University

- The discussion highlighted new studies that could provide data inputs to the Environmental Benefits Mapping and Analysis Program–Community Edition (BenMAP-CE) used for epidemiologic-based exposure-risk assessments to characterize health impacts in at-risk populations.
- Several new multicity and nationwide studies reported associations with O_3 exposure and respiratory outcomes (Strosnider et al. 2019; Bi et al. 2023; and Stowell et al. 2024).
- Several new studies assessed O_3 exposure and associations with social determinants of health effects at the neighborhood or zip code level (O'Lenick et al., 2017; Sheffield et al. 2019; Robles et al. 2023; and Klompmaker et al. 2021).
- Several recent national-level mortality studies of Medicare recipients assessed long-term effects of O_3 exposure at the individual and zip code levels with one study showing a protective effect.

Question 2: An important aspect in characterizing risk and making decisions regarding air quality standard levels is the shape of the *exposure-response relationships* for O_3 (based on the results from controlled human exposure studies) and the shape of the *concentration-response relationships* for O_3 (based on the epidemiologic studies). To what extent does new evidence made available since the last review inform our understanding of: (1) the potential for a concentration threshold in the O_3 concentration-response parameter; (2) the lowest concentrations from which one would specify the concentration-response parameter; (3) nonlinear parametric or nonparametric concentration-response functions at either low (i.e., <x) or high (i.e., >y) concentrations; (4) the appropriate time lag to specify when modeling O_3 mortality and morbidity effects; (5) the specific sensitivity analyses that would be appropriate to consider in support of uncertainty characterization for air quality epidemiologic-based assessments?

Lead Discussants: Kristen Rappazzo, U.S. EPA; Antonella Zanobetti, Harvard University

- In general, new epidemiologic studies focused on short-term effects have reported more linear concentration-response functions with no threshold.
- Recent studies of short-term effects of O_3 exposure indicated that effects were seen in the first one or two days for respiratory endpoints and had a lag of up to five days for cardiovascular endpoints. Variability has been reported for outcomes associated with birth and pregnancy. It was suggested that recent studies that reported on the synergistic effects of heat in the changing climate could change the lag period.
- The discussion highlighted the need for sensitivity analyses in support of uncertainty characterization for air quality epidemiologic-based assessment, including for consideration of different models and their impacts on thresholds; for studies to better control for factors like respiratory infections in their analyses; and for studies to consider differences between personal levels and ambient exposure levels when assessing dose-response concentrations.

Question 3: Is there new scientific evidence and/or new approaches, including joint effects and interaction models, that would support the estimation O_3-attributable risk for specific air quality scenarios independent of risk associated with exposure to other pollutants or stressors, such as temperature? How might epidemiologic studies specifying stressors including temperature or pollen as effect modifiers inform the EPA's understanding of the risks associated with O_3 exposure under a changing climate?

Lead Discussants: Neal Fann, U.S. EPA; Xiao Wu, Columbia University; Antonella Zanobetti, Harvard University

- A recent study (Coffman et al. 2024) employing BenMAP-CE to estimate the health impact associated with changes in multiple air pollutants, which used both a single and multipollutant approach, found that single-pollutant models are comparable with those quantified using a multipollutant model.
- Two recent studies assessed the interaction of O_3 with climate and environmental stressors, as well as synergistic effects of particulate matter and O_3 that could inform the EPA's understanding of the risks associated with O_3 exposure under a changing climate (Dominici et al. 2022; Liu et al. 2023).
- Accounting for temperature and other meteorological and regional parameters as effect modifiers of a number of O_3-attributable endpoints is important in epidemiologic-based risk assessments.

Question-and-Answer Session

Was a study area at elevation considered for inclusion in the 2020 assessment and will the upcoming review include one of these locations based on the higher O_3 levels at elevation?

- Both Denver and Salt Lake City were considered but not used. At the time, the modeling platform was new with lower performance and did not model those areas well.

Re: the APEX model, how did one uncertainty stem from the underestimation of autocorrection in individual behavior? Could the sensitivities be conducted with higher levels of autocorrelation to better simulate groups with significant time outside?

- This scenario is possible, and it would also be helpful to have more information on autocorrelation using real diaries.

Could heat index be used as an indicator of temperature stress on health outcomes?

- There do not appear to be any studies on this topic. Heat index is not the only measure of temperature; humidity is a summary measure and in a non-fixed relationship.

Appendix A: Attendance

U.S. EPA Planning Committee

Christine Alvarez
Project Manager
U.S. Environmental Protection Agency

Olivia Birkel
Project Manager Support
U.S. Environmental Protection Agency

Parker Duffney
Toxicologist
U.S. Environmental Protection Agency

Jeffrey Herrick
Ecologist
U.S. Environmental Protection Agency

Qingyu Meng
Physical Scientist
U.S. Environmental Protection Agency

Kristopher Novak
Ecologist
U.S. Environmental Protection Agency

Mary Hutson
Health Scientist
U.S. Environmental Protection Agency

Leigh Meyer, MS
Biologist
U.S. Environmental Protection Agency

Co-Chairs, Panelists, and Lead Discussants

Anne Barkley, PhD
Postdoctoral Research Scientist
U.S. Environmental Protection Agency

Mike Barna, PhD
Physical Scientist
National Park Service | Air Resources Division

Lisa Baxter, PhD
Director
U.S. Environmental Protection Agency

Michael Breen, PhD
Research Physical Scientist
U.S. Environmental Protection Agency

James Brown, PhD
Senior Health Scientist
U.S. Environmental Protection Agency

Peter Byrley, PhD
Physical Scientist
U.S. Environmental Protection Agency

Alex Carll, PhD
Assistant Professor
University of Louisville

Wayne Cascio, MD
Director, Center for Public Health, and Environmental Assessment
U.S. Environmental Protection Agency

Howard Chang, PhD
Professor
Emory University | Rollins School of Public Health

Olivia Clifton, PhD
Associate Research Scientist
Columbia University | NASA Goddard Institute for Space Studies

Evan Coffman, MPH
Epidemiologist
U.S. Environmental Protection Agency

Rebecca Dalton, PhD
Ecologist
U.S. Environmental Protection Agency

Jean-Jacques Dubois, PhD
Ecologist
U.S. Environmental Protection Agency

Parker Duffney, PhD
Toxicologist
U.S. Environmental Protection Agency

Steven Dutton, PhD
Division Director
U.S. Environmental Protection Agency

Lisa Emberson, PhD
Professor
University of York | Environment and Geography Department

Neal Fann, MPH
Senior Policy Analyst
U.S. Environmental Protection Agency

Aimen Farraj, PhD
Principal Investigator
U.S. Environmental Protection Agency

Daniel Goldberg, PhD
Assistant Research Professor
George Washington University | Department of Environmental and Occupational Health

Mehdi Hazari, PhD
Research Physiologist
U.S. Environmental Protection Agency

Barron Henderson, PhD
Physical Scientist
Air Quality Analysis Division | Air Quality Modeling Group of the Office of Air Quality Planning and Standard

Jeff Herrick, PhD
Ecologist
U.S. Environmental Protection Agency

Kirstin Hester, PhD
Biologist
U.S. Environmental Protection Agency

Mary Hutson, PhD
Health Scientist
U.S. Environmental Protection Agency

Dan Jaffe, PhD
Professor
University of Washington-Bothell | School of STEM | Physical Sciences Division

Annie Jarabek, PhD
Senior Science Advisor
U.S. Environmental Protection Agency

Scott Jenkins, PhD
Chief, Integrated Health Assessment Branch

U.S. Environmental Protection Agency

Michael Jerrett, PhD
Professor of Environmental Health Sciences
University of California – Los Angeles

Doug Kaylor, PhD
Ecologist
U.S. Environmental Protection Agency

Patrick Kinney, PhD/ScD
Beverly Brown Professor of Urban Health
Boston University, School of Public Health

Urmila Kodavanti, PhD
Research Biologist
U.S. Environmental Protection Agency

Alison Krajewski, PhD
Epidemiologist
U.S. Environmental Protection Agency

John Langstaff, MA
Environmental Scientist
U.S. Environmental Protection Agency

Meredith Lassiter, PhD
Ecologist
U.S. Environmental Protection Agency

David Lehmann, PhD
Toxicologist
U.S. Environmental Protection Agency

Danica Lombardozzi, PhD
Assistant Professor
Colorado State University | Ecosystem Science and Sustainability Department

Tom Long, PhD
Assistant Center Director
U.S. Environmental Protection Agency

Amy Luo
PhD Candidate, Ecology and Evolutionary Biology
University of Tennessee
Scientist in Park Intern
Great Smoky Mountain National Park

Jason Lynch, PhD
Ecologist
U.S. Environmental Protection Agency

Huiting Mao, PhD
Professor
State University of New York College of Environmental Science and Forestry | Department of Chemistry

Judit Marsillach, PhD
Assistant Professor
University of Washington School of Public Health | Department of Environmental and Occupational Health Sciences

Steve McDow, PhD
Physical Scientist
U.S. Environmental Protection Agency

Qingyu Meng, PhD
Physical Scientist
U.S. Environmental Protection Agency

Leigh Meyer, MS
Biologist
U.S. Environmental Protection Agency

Deirdre Murphy, PhD
U.S. Environmental Protection Agency

Kristopher Novak, PhD
Ecologist
U.S. Environmental Protection Agency

Dave Peden, MD
Professor, Dean for Translational Research, Medical Director
University of North Carolina at Chapel Hill

Robert Pinder, PhD
Supervisory Physical Scientist
U.S. Environmental Protection Agency

Sally Pusede, PhD
Associate Professor
University of Virginia | Department of Environmental Sciences

Havala Pye, PhD
Research Scientist
U.S. Environmental Protection Agency

Emmi Felker-Quinn, PhD
Ecologist
National Park Service | Air Resources Division

Kristen Rappazzo, PhD
Research Epidemiologist
U.S. Environmental Protection Agency

Susan Sachs
Education Branch Coordinator
Great Smoky Mountains National Park

Jason Sacks, MPH
Research Epidemiologist
U.S. Environmental Protection Agency

Sonja Sax, ScD
Environmental Health Scientist, Senior Consultant
Epsilon Associates, Inc.

Uma Shankar, PhD
Physical Scientist
U.S. Environmental Protection Agency

Tim Sharac, MS
Physical Scientist
U.S. Environmental Protection Agency

Drew Shindell, PhD
Nicholas Professor of Earth Science
Duke University

Sam Silva, PhD
Assistant Professor
University of Southern California

Heather Simon, PhD
Physical Scientist
U.S. Environmental Protection Agency

Travis Smith, PhD
Ecologist
U.S. Environmental Protection Agency

Susan Stone, MS
Senior Environmental Health Scientist
U.S. Environmental Protection Agency

Ripley Tisdale, PhD
USDA-ARS Research Plant Physiologist
Plant Science Research Unit

Gail Tonnesen, PhD
Environmental Engineer
U.S. Environmental Protection Agency | Region 8

William Vizuete, PhD
Professor
University of North Carolina at Chapel Hill | Gillings School of Global Public Health

Christopher Weaver, PhD
Division Director of the Integrated Climate Sciences Division
U.S. Environmental Protection Agency

Ben Wells
Statistician
U.S. Environmental Protection Agency

Jason West, PhD
Professor
University of North Carolina at Chapel Hill

Xiao Wu, PhD
Assistant Professor
Columbia University

Antonella Zanobetti, PhD
Principal Research Scientist
Harvard T.H. Chan School of Public Health

ICF Support

Janae Bonnell
Joshua Cleland
Tara Hamilton
Leah Hennelly
Aishwarya Javali
Kaedra Jones
Andrew Maresca
Lucas Melogno Rochas
Sheerin Shirajan
Harry Whately
Sam Whately

Appendix B: Simple Public Agenda

Workshop to Inform Review of the Ozone National Ambient Air Quality Standards

Agenda

Monday, May 13, 2024	
Timing	**Agenda Item**
9:50 AM – 10:00 AM	Host Opening
10:00 AM – 10:15 AM	Opening Remarks
10:15 AM – 10:30 AM	Welcome and Purpose of the Meeting
10:30 AM – 11:00 AM	Introduction to NAAQS
Session 1: Characterizing Ozone Chemistry and Transport, Air Quality Patterns, and Ozone as a Greenhouse Gas	
11:00 AM – 11:15 AM	Session Chair Introduction to Topics, Discussion Questions, and Panel
11:15 AM – 12:00 PM	Topic 1: Ozone Chemistry and Transport and Resulting Concentration Patterns
12:00 PM – 12:45 PM	Topic 2: Current State of U.S. Emissions and Connection to Health and Environmental Justice
12:45 PM – 1:00 PM	Questions and Answer Session
1:00 PM – 1:30 PM	Lunch
1:30 PM – 2:15 PM	Topic 3: Monitoring and Modeling Advances
2:15 PM – 3:00 PM	Topic 4: Background Ozone Concentrations
3:00 PM – 3:45 PM	Topic 5: Ozone as a Greenhouse Gas
3:45 PM – 4:00 PM	Questions and Answer Session
4:00 PM	Day 1 Adjournment
Tuesday, May 14, 2024	
10:00 AM – 10:10 AM	Host Opening
10:10 AM – 10:15 AM	Opening Remarks
Session 1: Planning for the Review of the Welfare Effects Evidence and Analyses Review of welfare effects evidence	
10:15 AM – 10:30 AM	Session Chair Introduction to Topics, Discussion Questions, and Panel
10:30 AM – 11:00 AM	Topic 1: Ecosystem Processes
11:00 AM – 11:30 AM	Topic 2: Community Level Effects
11:30 AM – 12:00 PM	Topic 3: Population/Individual Level Effects
12:00 PM – 12:30 PM	Topic 4: Exposure/Dose-Response
12:30 PM – 1:00 PM	Topic 5: Climate and Other Modifying Factors
1:00 PM – 1:15 PM	Questions and Answer Session
1:15 PM – 2:00 PM	Lunch
2:00 PM – 4:15 PM	**Session 2: Welfare Risk and Exposure Assessment**
4:15 PM – 4:30 PM	Questions and Answer Session
4:30 PM	Day 2 Adjournment

Wednesday, May 15, 2024	
Timing	**Agenda Item**
9:50 AM – 10:00 AM	Host Opening
10:00 AM – 10:15 AM	Opening Remarks
Session 1: Human Exposure to Ambient O_3	
10:15 AM – 10:30 AM	Session Chair Introduction to Topics, Discussion Questions, and Panel
10:30 AM – 11:15 AM	Topic 1: Exposure Surrogates, Errors, and Measurement/Modeling Approaches
11:15 AM – 11:45 AM	Topic 2: Exposure to O3 in a Multipollutant Environment
11:45 AM – 12:00 PM	Questions and Answer Session
12:00 PM – 12:30 PM	Lunch
Session 2: Planning for the Review of Health Effects Evidence – Emerging Evidence and Interpretation	
12:30 PM – 12:45 PM	Session Chair Introduction to Topics, Discussion Questions, and Panel
12:45 PM – 2:15 PM	Topic 1: Emerging Evidence, Health Outcomes, and Methods
2:15 PM – 3:15 PM	Topic 2: Interpretation of Evidence
3:15 PM – 5:00 PM	**Session 3: Planning for the Review of Health Effects Evidence – Evidence Integration**
5:00 PM – 5:15 PM	Questions and Answer Session
5:15 PM	Day 3 Adjournment
Thursday, May 16, 2024	
9:50 AM – 10:00 AM	Host Opening
10:00 AM – 10:15 AM	Opening Remarks
Session 1: Planning for the Review of Health Effects Evidence: Public Health Implications	
10:15 AM – 10:30 AM	Session Chair Introduction to Topics, Discussion Questions, and Panel
10:30 AM – 11:20 AM	Topic 1: At-Risk Populations
11:20 AM – 11:40 AM	Topic 2: Concentration Response
11:40 AM – 11:55 AM	Questions and Answer Session
11:55 AM – 12:30 PM	Lunch
Session 2: Planning for the Review of Human Exposure and Health Risk Assessments	
12:30 PM – 12:45 PM	Session Chair Introduction to Topics, Discussion Questions, and Panel
12:45 PM – 1:15 PM	Topic 1: Estimating Ambient Air Concentrations
1:15 PM – 1:45 PM	Topic 2: Estimating Exposure Concentrations
1:45 PM – 2:15 PM	Topic 3: Lung Function Risk Analysis
2:15 PM – 2:35 PM	Topic 4: Exposure to Benchmark Analyses
2:35 PM – 3:35 PM	Topic 5: Air Quality Epidemiologic-Based Assessment
3:35 PM – 3:50 PM	Questions and Answer Session
3:50 PM – 4:00 PM	Closing Remarks and Adjournment

Monday, May 13, 2024	
Timing (ET)	**Agenda Item**
9:50 AM – 10:00 AM	Host Opening
10:00 AM – 10:15 AM	Opening Remarks
10:15 AM – 10:30 AM	Welcome and Purpose of the Meeting
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12:45 PM – 1:00 PM	Questions and Answer Session
1:00 PM – 1:30 PM	Lunch
1:30 PM – 2:15 PM	Topic 3: Monitoring and Modeling Advances Relevant to Welfare
2:15 PM – 3:00 PM	Topic 4: Background Ozone Concentrations
3:00 PM – 3:45 PM	Topic 5: Ozone as a Greenhouse Gas
3:45 PM – 4:00 PM	Questions and Answer Session
4:00 PM	Day 1 Adjournment
Tuesday, May 14, 2024	
10:00 AM – 10:10 AM	Host Opening
10:10 AM – 10:15 AM	Opening Remarks
Session 1: Planning for the Review of the Welfare/Ecological Effects Evidence	
10:15 AM – 10:30 AM	Session Chair Introduction to Topics, Discussion Questions, and Panel
10:30 AM – 11:00 AM	Topic 1: Ecosystem Processes
11:00 AM – 11:30 AM	Topic 2: Community Level Effects
11:30 AM – 12:00 PM	Topic 3: Population/Individual Level Effects
12:00 PM – 12:30 PM	Topic 4: Exposure/Dose-Response
12:30 PM – 1:00 PM	Topic 5: Climate and Other Modifying Factors
1:00 PM – 1:15 PM	Questions and Answer Session
1:15 PM – 2:00 PM	Lunch
2:00 PM – 4:15 PM	**Session 2: Welfare Risk and Exposure Assessment**
4:15 PM – 4:30 PM	Questions and Answer Session
4:30 PM	Day 2 Adjournment

Appendix C: Detailed Agenda for Chairs/Panelists:

Day 1, May 13, 2024[1]

Timing	Agenda Item
9:50 – 10:00 a.m. ET	**Host Opening [ICF]**
10:00 – 10:15 a.m. ET	**Opening Remarks [Chris Frey, U.S. EPA]**
10:15 – 10:30 a.m. ET	**Welcome and Purpose of the Meeting [Steve Dutton, Chris Weaver and Erika Sasser, U.S. EPA]**
10:30 – 11:00 a.m. ET	**Introduction to NAAQS [OAR and ORD, U.S. EPA]**

Session 1: Characterizing Ozone Chemistry and Transport, Air Quality Patterns, and Ozone as a Greenhouse Gas (11:00 am – 3:45 pm)

Session Co-chairs: Anne Barkley (EPA), Olivia Clifton (NASA-GISS/Columbia)

Panelists: Havala Pye (EPA), Barron Henderson (EPA), Heather Simon (EPA), Gail Tonnesen (EPA Region 8), Olivia Clifton (NASA-GISS/Columbia), Dan Jaffe (Univ. Wash.), Daniel Goldberg (GWU), Sally Pusede (UVA), Sam Silva (USC (Cali)), William Vizuete (UNC), Jason West (UNC), Uma Shankar (EPA), Mike Barna (NPS), Drew Shindell (Duke), Peter Byrley (EPA), Chris Weaver (EPA), Rob Pinder (EPA), Jeff Herrick (EPA)

11:00 – 11:15 a.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
11:15 a.m. – 12:00 p.m. ET Topic 1	**Topic 1:** Ozone Chemistry and Transport and Resulting Concentration Patterns • What new information is available and what are the most significant advances in theoretical chemistry, kinetics and smog chamber work, field experiments, ambient monitoring, satellite observations, and numerical modeling that improve our current understanding of O_3 production, loss, and transport? What are the implications of this new information? **Lead discussants assigned:** Sally Pusede (UVa) and Havala Pye (EPA)
12:00 – 12:45 p.m. ET Topic 2	**Topic 2:** Current State of U.S. Emissions and Connection to Health and Environmental Justice • What new information is available to inform how O_3 versus total oxidant exposure differ across spatial scales, particularly in urban areas where O_3 concentrations are low because of reactions with NO and where environmental

[1] Participation time is set to eastern standard time.

Session 1: Characterizing Ozone Chemistry and Transport, Air Quality Patterns, and Ozone as a Greenhouse Gas (11:00 am – 3:45 pm)	
	justice concerns are particularly important? What metrics are available to accurately describe the relationship between O_3 and total oxidant exposure; for example, could a combination of indicators be used? **Lead discussants assigned:** William Vizuete (UNC) and Gail Tonnesen (EPA Region 8)
12:45 – 1:00 p.m. ET	**Questions and Answer Session**
1:00 – 1:30 p.m. ET	**Lunch**
1:30 – 2:15 p.m. ET Topic 3	**Topic 3:** Monitoring and Modeling Advances Relevant to Welfare • What recent advances have been made in monitoring and modeling concentrations of O_3? How accurate are recently developed modeling approaches (including hybrid models that utilize data from satellites, land use information, ground-based monitors, etc.) at predicting O_3 emissions and O_3 concentrations across locations (e.g., urban vs. rural, monitored vs. unmonitored)? What have the new advances contributed to characterizing and understanding sources and precursors (e.g., wildfires, oil and gas emissions, intercontinental transport, etc.) that contribute to ambient O_3, particularly in the west and intermountain west where O_3 has an impact on sensitive ecosystems? **Lead discussants assigned**: Dan Goldberg (GWU) and Heather Simon (EPA)
2:15 – 3:00 p.m. ET Topic 4	**Topic 4: Background Ozone Concentrations** • What new information is available on characterizing or estimating background O_3 concentrations (e.g., including hybrid methods)? What have new advances in monitoring and modeling contributed to characterizing sources and precursors (e.g., wildfires, intercontinental transport, stratosphere-troposphere exchange, etc.) that contribute to background O_3 concentrations? Is there new information on atmospheric transport, chemistry, and concentration trends that can be used to reduce uncertainties in seasonal or daily background O_3 estimates? **Lead discussants assigned**: Dan Jaffe (Univ Wash) and Barron Henderson (EPA)
3:00 – 3:45 p.m. ET	**Topic 5: Ozone as a Greenhouse Gas** • How have modeling studies conducted since the previous Ozone ISA changed the ISA conclusions regarding the response of the climate system to O_3 impacts? What new information is there on the role of regional and seasonal variations in the atmospheric budgets of O_3 and therefore on its climate impacts? What new information is there

Session 1: Characterizing Ozone Chemistry and Transport, Air Quality Patterns, and Ozone as a Greenhouse Gas (11:00 am – 3:45 pm)	
	on the impact of O_3 on the terrestrial ecosphere and its climate feedback? What is the role of precursors in the climate impacts of O_3 under possible future emission scenarios? **Lead discussants assigned**: Jason West (UNC) and Uma Shankar (EPA)
3:45 – 4:00 p.m. ET	**Questions and Answer Session**
4:00 p.m. ET	**Adjourn [ICF]**

Day 2, May 14, 2024[2]

Timing	Agenda Item
10:00 – 10:10 a.m. ET	**Host Opening [ICF]**
10:10 – 10:15 a.m. ET	**Opening Remarks [Liz Naess, U.S. EPA]**

Session 1: Planning for the Review of the Welfare/Ecological Effects Evidence (10:15 am – 1:00 pm)

Session Co-chairs: Jeffrey Herrick/Kris Novak (EPA), Emmi Felker-Quinn (NPS)

Panelists: Doug Kaylor (EPA), Jason Lynch (EPA), Meredith Lassiter (EPA), Jean-Jacques Dubois (EPA), Olivia Clifton (NASA), Danica Lombardozzi (CO State), Huiting Mao (SUNY-ESF), Lisa Emberson (Univ of York, UK), Ripley Tisdale (USDA), Susan Sachs (NPS), Amy Luo (Univ of TN)

10:15 – 10:30 a.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
10:30 – 11:00 a.m. ET Topic 1	**Topic 1: Ecosystem Processes** • What new information is available about ozone effects on ecosystem processes such as water cycling, carbon sequestration, productivity, and belowground/biogeochemical cycling? **Lead discussants assigned**: Danica Lombardozzi (CO State) and Doug Kaylor (EPA) **Question panel:** Lisa Emberson (Univ of York, UK), Emmi Felker-Quinn (NPS), Jason Lynch (EPA), Jeffrey Herrick (EPA)
11:00 – 11:30 a.m. ET Topic 2	**Topic 2: Community-Level Effects** • What new information is available about ozone effects at the community level such as biodiversity, community composition, and species interactions? • What new information is available on ozone effects on volatile plant

[2] Participation time is set to eastern standard time.

Session 1: Planning for the Review of the Welfare/Ecological Effects Evidence (10:15 am – 1:00 pm)	
	signaling compounds and plant-insect signaling? **Lead discussants assigned**: Emmi Felker-Quinn (NPS) and Meredith Lassiter (EPA) **Question panel:** Lisa Emberson (Univ of York, UK), Doug Kaylor (EPA)
11:30 a.m. – 12:00 p.m. ET Topic 3	**Topic 3: Population/ Individual Level Effects** • What new information is available about ozone effects at the population or individual level such as survival, growth, reproduction, phenology, visible foliar injury, and crop yield? • In particular, is there new information on non-tree species, non-commodity crops, and species that are threatened and endangered or culturally significant? • What new information is available on ozone effects on insect herbivores and other wildlife? **Lead discussants assigned**: Ripley Tisdale (USDA) and Jean-Jacques Dubois (EPA) **Question panel:** Jason Lynch (EPA), Doug Kaylor (EPA), Meredith Lassiter (EPA), Susan Sachs (NPS), Amy Luo (Univ of TN)
12:00 – 12:30 p.m. ET Topic 4	**Topic 4: Exposure/ Dose Response** • What new information is available on linking concentration weighted metrics (e.g., W126 & AOT40) to response of species found in the United States? • Is there new information linking flux metrics to effects on species that occur in the United States? **Lead discussants assigned:** Lisa Emberson (Univ of York, UK) and Jeff Herrick (EPA) **Question panel:** Emmi Felker-Quinn (NPS), Olivia Clifton (NASA), Jean-Jacques Dubois (EPA), Huiting Mao (SUNY-ESF)
12:30 – 1:00 p.m. ET	**Topic 5: Climate and Other Modifying Factors** • Is there new information on how ozone's effects on ecosystems and their components are modified by climate change and other factors (e.g., temperature, soil moisture, nutrients, and/or other pollutants)? **Lead discussants assigned**: Jason Lynch (EPA) and Kris Novak (EPA) **Question panel:** Emmi Felker-Quinn (NPS), Doug Kaylor (EPA), Danica Lombardozzi (CO State)
1:00 – 1:15 p.m. ET	**Questions and Answer sessions**
1:15 – 2:00 p.m. ET	**Lunch**

Session 2: Welfare Risk and Exposure Assessment (2:00 – 4:15 p.m. ET)

Session Co-chairs: Leigh Meyer (EPA), Kris Novak (EPA)
Panelists: Travis Smith (EPA), Deirdre Murphy (EPA), Jason Lynch (EPA), Kris Novak (EPA), Heather Simon (EPA), Ben Wells (EPA), Susan Stone (EPA), Barron Henderson (EPA), Jean-Jacques Dubois (EPA), Jeffrey Herrick (EPA), Tim Sharac (EPA), Rachel Sales (EPA), Emmi Felker-Quinn (NPS), Olivia Clifton (NASA-GISS/Columbia), Huiting Mao (SUNY-ESF), Lisa Emberson (Univ of York, UK), Will Vizuete (UNC), Dan Jaffe (Univ. of Wash), Sally Pusede (UVa), Drew Shindell (Duke), Susan Sachs (NPS), Amy Lou (Univ of TN), Ripley Tisdale (USDA)

2:00 – 2:15 p.m. ET

Session Chair Introduction to Topics, Discussion Questions, and Panel

2:15 – 2:45 p.m. ET

- Ozone concentration gradients exist across the US and are influenced by the location of emission sources and ozone chemistry and transport. Reflecting those concentration gradients can be important in understanding the protection provided by the ozone standard. What modeling approaches are available and might be employed to estimate ambient air O_3 concentrations across large areas, including forested areas and the sources that influence air quality in these areas? What is an appropriate approach to model or estimate O_3 impacts upwind of urban areas?
    - How might this be done to simulate different air quality scenarios, including one for when the design value is just meeting the current standard?
    - What kind of case study areas or parts of the United States might be appropriate to include in this assessment?

Lead discussants assigned: Ben Wells (EPA), Barron Henderson (EPA), Olivia Clifton (NASA-GISS/Columbia), Will Vizuete (UNC)

2:45 – 3:15 p.m. ET

- How might climate change (e.g., temperature, precipitation changes) be reflected in the air quality scenarios included in the risk and exposure assessment? Are there climate change policies that should be accounted for in the assessment? What analytical approaches could be used to assess the influence of current climate change on risks to vegetation?

Lead discussants assigned: Rachel Sales (EPA) and Drew Shindell (Duke)

3:15 – 3:45 p.m. ET

- Recognizing the important role that species-specific exposure-response functions have played in past reviews, are there new data or information that should be incorporated to improve our understanding of these data and resulting exposure-response functions? Are there different analytical approaches that should be utilized?
    - Are there other approaches that should be considered, including approaches that might incorporate metrics for both peak concentrations and for cumulative/sustained exposures on tree seedling biomass?
    - How can the dataset be analyzed differently to provide a clearer understanding of the patterns of ambient air O_3 concentrations common today (e.g., reduced prevalence of peak concentrations)?

Lead discussants assigned: Travis Smith (EPA) and Lisa Emberson (Univ of York, UK)

Session 2: Welfare Risk and Exposure Assessment (2:00 – 4:15 p.m. ET)	
3:45 – 4:15 p.m. ET	• What approaches and methods are available that estimate O_3 tree community forest impacts (e.g., species diversity and richness) considering interspecies competition and other interactions? For example, what are current methods for modeling O_3 concentration scenarios against tree species competition over a period of time? What are their strengths and limitations? ○ Are studies, methods, or approaches available that might be used to relate extent and magnitude of foliar injury in forested areas to public uses/values and ecosystem services that might inform judgments of public welfare significance? **Lead discussants assigned**: Kris Novak (EPA) and Emmi Felker-Quinn (NPS)
4:15 – 4:30 p.m. ET	**Questions and Answer Session**
4:30 p.m. ET	**Adjourn [ICF]**

Day 3, May 15, 2024[3]

Timing	Agenda Item
9:50 – 10:00 a.m. ET	**Host Opening [ICF]**
10:10 – 10:15 a.m. ET	**Opening Remarks [Steve Dutton, U.S. EPA]**

Session 1: Human Exposure to Ambient O_3 (10:15 a.m. – 11:45 a.m.)

Session Co-chairs: Peter Byrley (EPA), Michael Jerrett (UCLA)

Panelists: Lisa Baxter (EPA), Jeffrey Brook (U. Toronto), Peter Byrley (EPA), Michael Jerrett (UCLA), Patrick Kinney (Boston U), Sonja Sax (Epsilon Associates Inc.), Gail Tonnesen (EPA Region 8), William Vizuete (UNC)

10:15 – 10:30 a.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
10:30 – 11:15 a.m. ET Topic 1	**Topic 1: Exposure Surrogates, Errors, and Measurement/Modeling Approaches** • What new information is available on the relationship between ambient ozone concentrations and personal exposures in various microenvironments, including infiltration from outdoor to indoor environments? What new information is available to improve our understanding of the discrepancies between stationary monitor measurements and actual pollutant exposures? What recent advances have been made in monitoring and modeling (including hybrid models that utilize data from satellites, land use information, ground-based monitors, etc.) ambient concentrations of ozone across locations (e.g., urban vs. rural, monitored vs. unmonitored) to improve understanding of human exposures? How have these approaches been evaluated and validated in various types of locations (e.g., urban vs. rural, monitored vs. unmonitored)? **Lead discussants assigned**: Michael Jerrett (UCLA), Lisa Baxter (EPA)
11:15 – 11:45 a.m. ET Topic 2	**Topic 2: Exposure to O_3 in a Multipollutant Environment** • What new information from measurement and modeling approaches is available to characterize the relationships between ozone exposures and exposures to other ambient air pollutants? Does this new information provide insight into the potential for co-pollutants confounding health studies. **Lead discussants assigned**: Jeffrey Brook (Univ. Toronto), Peter Byrley (EPA)
11:45 a.m. – 12:00 p.m. ET	**Questions and Answer Session**
12:00 – 12:30 p.m. ET	**Lunch**

[3] Participation time is set to eastern standard time.

Session 2: Planning for the Review of Health Effects Evidence: **Emerging Evidence and Interpretation (12:30 – 3:15 p.m. ET)** **Session Co-chairs:** David Lehmann (EPA), Howard Chang (Emory University) **Panelists:** Kristen Rappazzo (EPA), Aimen Farraj (EPA), Mehdi Hazari (EPA), Lisa Baxter (EPA), James Brown (EPA), Evan Coffman (EPA), Kirstin Hester (EPA), Alison Krajewski (EPA), Annie Jarabek (EPA), Parker Duffney (EPA), David Lehmann (EPA), Howard Chang (Emory University), Michael Jerrett (UCLA), Antonella Zanobetti (Harvard University), Judit Marsillach (University of Washington), Patrick Kinney (Boston University), Sonja Sax (Epsilon), Alex Carll (University of Louisville), David Peden (University of North Carolina), Jason West (University of North Carolina)	
12:30 – 12:45 p.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
Topic 1: Emerging Evidence, Health Outcomes, and Methods (12:45 – 2:15 p.m. ET)	
12:45 – 1:15 p.m. ET Topic 1	• The last O_3 ISA evaluated evidence for respiratory effects, cardiovascular effects, metabolic-related health outcomes, reproductive and developmental outcomes, nervous system effects, cancer, and mortality. Since the last review, what new or emerging O_3-related health effect endpoints have been evaluated in epidemiologic, controlled human exposure, or animal toxicological studies (e.g., cognitive decline, autism, immune effects)? Is there new evidence that further informs endpoints included in the 2020 ISA. Specifically, is there new evidence 1) that is consistent with causality determinations in the 2020 ISA, 2) that contradicts causality determinations in the 2020 ISA, or 3) that further improves the understanding of biological plausibility, health outcomes for at-risk populations, and health outcomes at lower O_3 concentrations? **Lead discussants assigned**: Parker Duffney (EPA), Alex Carll (University of Louisville)
1:15 – 1:45 p.m. ET	• Have recent controlled human exposure or animal toxicological studies examined the potential mechanisms of action by which short-term and/or long-term O_3 exposures may result in health effects, particularly cardiovascular effects and other effects not determined to be “causal” in previous ISAs? Do recent experimental studies provide insights into the biological plausibility of these O_3-induced effects? **Lead discussants assigned**: Aimen Farraj (EPA), David Peden (University of North Carolina)
1:45 – 2:15 p.m. ET	• What new or emerging methodologies or study designs are available in epidemiology to (1) address potential effect modifiers (e.g., genetic traits and socioeconomic status) and confounders (both chemical and nonchemical stressors), (2) disentangle the effects of long-term exposure and short-term exposure to O_3, (3) better understand potential heterogeneity in O_3 effects assessed in U.S. multicity studies,

Session 2: Planning for the Review of Health Effects Evidence:	
	and (4) understand the role of O_3 as a mediator? **Lead discussants assigned**: Howard Chang (Emory University), Kristen Rappazzo (EPA)
Topic 2: Interpretation of Evidence (2:15 – 3:15 p.m. ET)	
2:15 – 2:45 p.m. ET	• What factors are important to consider when evaluating epidemiologic studies conducted in geographic regions less representative of conditions in the United States (e.g., In terms of sources, air quality mixtures, exposure patterns, population characteristics)? **Lead discussants assigned**: Lisa Baxter (EPA), Antonella Zanobetti (Harvard University)
2:45 – 3:15 p.m. ET	• To what extent is new scientific evidence becoming available from experimental or epidemiologic studies to improve the understanding of effects associated with various patterns of O_3 exposure (e.g., repeated short-term exposures to "peak" concentrations versus longer-term exposures to "average" concentrations)? **Lead discussants assigned**: James Brown (EPA), Kristen Rappazzo (EPA)

Session 3: Planning for the Review of Health Effects Evidence: Evidence Integration (3:15–5:00 p.m. ET)

Session Co-chairs: Parker Duffney (EPA), Dave Peden (UNC)

Panelists: Kristen Rappazzo (EPA), Aimen Farraj (EPA), Mehdi Hazari (EPA), Lisa Baxter (EPA), Jim Brown (EPA), Parker Duffney (EPA), David Lehmann (EPA), Kirstin Hester (EPA), Evan Coffman (EPA), Alison Krajewski (EPA), Anne Barkley (EPA), Michael Jerrett (UCLA), Howard Chang (Emory), Antonella Zanobetti (Harvard), Judit Marsillach (University of Washington), Sonja Sax (Epsilon), Patrick Kinney (Boston U), Alex Carll (U. Louisville), Dave Peden (UNC), Annie Jarabek (EPA), Jason West (UNC)

3:15 – 3:30 p.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
3:30 – 4:00 p.m. ET	• To what extent do recent advances in the ozone health effects evidence support integration of findings across epidemiology, controlled human exposure, animal toxicology, and dosimetry? What does the new evidence indicate regarding consistency of findings within disciplines (e.g., epidemiology studies of cardiovascular mortality versus morbidity)? To what extent do recent ozone health effects findings from a particular discipline compensate for data gaps in other disciplines? **Lead discussants assigned**: Parker Duffney (EPA), Michael Jerrett (UCLA)

Session 3: Planning for the Review of Health Effects Evidence: Evidence Integration (3:15–5:00 p.m. ET)	
4:00 – 4:30 p.m. ET	• What limitations are present in experimental studies that expose humans or animals to “pure” ozone rather than to the ambient mix of ozone and related photochemical oxidants (plus other co-occurring pollutants)? Is there new information available for us to better understand the health effects of photochemical oxidants other than O_3 in ambient air? **Lead discussants assigned**: Mehdi Hazari (EPA), Anne Barkley (EPA)
4:30 – 5:00 p.m. ET	• In the 2020 Ozone ISA, experimental studies were considered for inclusion if subjects were exposed to ozone concentrations less than or equal to 2 ppm (in animals) or 0.4 ppm (in humans). These limits were based on findings that the deposition of ozone from a 2-hour exposure to 2 ppm ozone in a resting rat is roughly equivalent to deposition of ozone resulting from a 2-hour exposure to 0.4 ppm in an exercising human (Hatch et al., 1994). Is there new or other data that can inform the potential human health implications of animal studies of shorter-term, but higher ozone concentration? How can recent animal studies examining ozone exposures well above ambient concentrations inform human responses near the level of the current standard? **Lead discussants assigned**: James Brown (EPA), Annie Jarabek (EPA)
5:00 – 5:15 p.m. ET	**Questions and Answer Session**
5:15 p.m. ET	**Adjourn [ICF]**

Day 4, May 16, 2024[4]

Timing	Agenda Item
9:50 – 10:00 a.m. ET	**Host Opening [ICF]**
10:10 – 10:15 a.m. ET	**Opening Remarks [Wayne Cascio, U.S. EPA]**

Session 1: Planning for the Review of Health Effects Evidence: Public Health Implications (10:15 a.m. – 11:55 a.m.) **Session Co-chairs:** Alison Krajewski (EPA), and Jason Sacks (EPA) **Panelists:** Jason Sacks (EPA), Kristen Rappazzo (EPA), Urmila Kodavanti (EPA), Aimen Farraj (EPA), Mehdi Hazari (EPA), James Brown (EPA), Wayne Cascio (EPA), Evan Coffman (EPA), Kirstin Hester (EPA), Parker Duffney (EPA), David Lehmann (EPA), Alison Krajewski (EPA), Lisa Baxter (EPA), Howard Chang (Emory), Michael Jerrett (UCLA), Antonella Zanobetti (Harvard), Judit Marsillach (University of Washington), Patrick Kinney (Boston University), Sonja Sax (Epsilon), Alex Carll (U. Louisville), David Peden (UNC), Jason West (UNC)	
10:15 – 10:30 a.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
Topic 1: At-Risk Populations	
10:30 – 10:50 a.m. ET	• To what extent is new evidence available to inform the understanding of subpopulations that are particularly at increased risk to O_3 exposures? How can recent evidence from epidemiologic, controlled human exposure, and animal toxicological studies be used to inform conclusions related to at-risk populations, such as genetic traits that may underlie increased risk or additional life stages or populations (e.g., preexisting diseases such as diabetes) potentially at increased risk of an O_3-related health effect? How can recent health effects evidence in particular populations be integrated with other health information (e.g., mechanistic and biological plausibility information) to better understand the public health impacts of O_3 exposure? **Lead discussants assigned**: Jason Sacks (EPA), Patrick Kinney (Boston U)
10:50 – 11:20 a.m. ET	• Is there new information that identifies a combination of risk factors that can lead to one or more life stages or populations being at greater risk compared to another? What new experimental and observational studies are available to improve our understanding of critical exposure windows? **Lead discussants assigned**: Kristen Rappazzo (EPA) and Judit Marsillach (U Washington)

[4] Participation time is set to eastern standard time.

Session 1: Planning for the Review of Health Effects Evidence: Public Health Implications (10:15 a.m. – 11:55 a.m.)

Topic 2: Concentration Response

11:20 – 11:40 a.m. ET	• How do the results of recent studies inform the shapes of the concentration-response relationships for O_3 and various health outcomes (e.g., mortality, hospital admissions, etc.), especially for exposures relevant to O_3 concentrations near the current O_3 NAAQS? **Lead discussants assigned**: Antonella Zanobetti (Harvard) and Lisa Baxter (EPA)
11:40 – 11:55 a.m. ET	**Questions and Answer Session**
11:55 a.m. – 12:30 p.m. ET	**Lunch**

Session 2: Planning for the Review of Human Exposure and Health Risk Assessments (12:30 – 3:50 p.m. ET)

Session Co-chairs: Mary Hutson (EPA), Tom Long (EPA)

Panelists: Heather Simon (EPA), John Langstaff (EPA), Michael Breen (EPA), Neal Fann (EPA), Barron Henderson (EPA), Jim Brown (EPA), Ben Wells (EPA), Jen Sellers (EPA), Kristen Rappazzo (EPA), Susan Stone (EPA), Henry Raab (EPA), William Vizuete (UNC), Sonya Sax (Epsilon), Michael Jerrett (UCLA), Antonella Zanobetti (HSPS), Dave Peden (UNC), Howard Chang (Emory), Xiao Wu (Columbia), Alex Carll (University of Louisville), Sally Pusede (UVA)

12:30 – 12:45 p.m. ET	**Session Chair** Introduction to Topics, Discussion Questions, and Panel
12:45 – 1:15 p.m. ET	**Topic 1: Estimating Ambient Air Concentrations** • Are there new approaches or improvements to estimating ambient concentrations for input into the exposure modeling and epidemiologic-based risk assessment, including O_3 concentrations representing recent conditions and O_3 concentrations just meeting objectives for each air quality scenario that may be appropriate to consider in this review? Specifically, is there new scientific evidence that can help refine spatial and temporal estimates of O_3 concentrations and/or inform estimates of changing O_3 concentrations due to emissions reductions? **Lead Discussants Assigned:** Heather Simon (EPA), William Vizuete (UNC) Ben Wells (EPA)
1:15 – 1:45 p.m. ET	**Topic 2: Estimating Exposure Concentrations** • Are there new scientific developments related to the major components of exposure modeling, including inputs to the model (e.g., microenvironmental concentrations, human activity patterns,

Session 2: Planning for the Review of Human Exposure and Health Risk Assessments (12:30 – 3:50 p.m. ET)	
	differential exposures to population groups, air exchange rate distributions, and indoor air chemistry) that are appropriate for EPA to consider in its assessment planning? Especially for the APEX model, is there new scientific evidence available that may be appropriate to consider, such as new approaches or tools for evaluating APEX performance (e.g., sensitivity analysis, field studies)? **Lead Discussants Assigned:** John Langstaff (EPA), Alex Carll (University of Louisville), Michael Breen (EPA)
1:45 – 2:15 p.m. ET	**Topic 3: Lung Function Risk Analysis:** • Is there new information that would lessen uncertainties in the lung function models, particularly uncertainties related to exposure circumstances less well studied in the controlled human exposure experiments (e.g., response to low exposures and with low ventilation rates)? Are there approaches or information regarding inter-individual variability in lung function that would support uncertainty and variability characterization for O_3-attributable lung function risk estimates? **Lead Discussants Assigned:** Jim Brown (EPA), Jen Sellers (EPA), Sonja Sax (Epsilon)
2:15 – 2:35 p.m. ET	**Topic 4: Exposure to Benchmark Analyses** • Is there new scientific evidence (e.g., human exposure studies, panel studies) that EPA should consider to inform benchmark O_3 concentrations, exposure duration and/or at-risk populations evaluated in the population exposure to benchmark comparison analysis? **Lead Discussants Assigned**: John Langstaff (EPA) Dave Peden (UNC), Sonja Sax (Epsilon)
Topic 5: Air Quality Epidemiologic-Based Assessment	
2:35 – 2:55 p.m. ET	• Do new studies exist that would permit EPA to estimate risks in specific at-risk populations? **Lead Discussants Assigned**: Neal Fann (EPA), Michael Jerrett (UCLA), Howard Chang (Emory)
2:55 – 3:25 p.m. ET	• An important aspect in characterizing risk and making decisions regarding air quality standard levels is the shape of the *exposure-response relationships* for O_3 based on the results from controlled human exposure studies and the shape of the *concentration-response relationships* for O_3 based on the epidemiologic studies. To what extent does new evidence made available since the last review inform our understanding of: (1) the potential for a concentration threshold in the ozone concentration-response parameter; (2) the lowest concentrations from which one would specify the concentration-

Session 2: Planning for the Review of Human Exposure and Health Risk Assessments (12:30 – 3:50 p.m. ET)	
	response parameter; (3) nonlinear parametric or nonparametric concentration-response functions at either low (i.e., <x) or high (i.e., >y) concentrations; (4) the appropriate time lag to specify when modeling ozone-mortality and morbidity effects?; 5) what specific sensitivity analyses would be appropriate to consider in support of uncertainty characterization for air quality epidemiologic-based assessments? **Lead Discussants Assigned**: Kristen Rappazzo (EPA), Antonella Zanobetti (HSPH)
3:25 – 3:45 p.m. ET	• Is there new scientific evidence and/or new approaches including joint effects and interaction models that would support the estimation O_3-attributable risk for specific air quality scenarios independent of risk associated with exposure to other pollutants or stressors, such as temperature? How might epidemiologic studies specifying stressors including temperature or pollen as effect modifiers inform EPA's understanding of the risks associated with ozone exposure under a changing climate? **Lead Discussants Assigned**: Neal Fann (EPA), Xiao Wu (Columbia), Antonella Zanobetti (HSPH)
3:45 – 4:00 p.m. ET	**Questions and Answer Session**
4:00 – 4:05 p.m. ET	**Closing Remarks/Adjourn [EPA]**

Bibliography

Characterizing Ozone Chemistry and Transport, Air Quality Patterns, and Ozone as a Greenhouse Gas – May 13, 2024

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