North American Chapter of the International Society For Environmental Epidemiology
OMB Call on EPA Ozone Standard Setting
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Speaker 1: Dr. Marianthi-Anna Kioumourtzoglou
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Introduction: What is ozone air pollution?

Ozone is a powerful oxidant and toxic air pollutant. It is composed of three oxygen atoms. Ozone in the upper atmosphere, i.e., in the stratosphere (aka the ozone layer), protects life on Earth from too much ultraviolet radiation from the sun. For this reason, stratospheric ozone is also called "good ozone." However, ozone at ground level (i.e., tropospheric ozone) is a harmful air pollutant ("bad ozone") due to its impacts on human health and the environment and it's one of the main smog elements.

Tropospheric ozone is a secondary pollutant; that is, it does not have direct emission sources. It is formed secondarily in the atmosphere, in presence of heat and sunlight, by chemical reactions of its precursors, nitrogen oxides (NOx) and volatile organic compounds (VOCs). The main emission sources of the ozone precursors NOx and VOCs are cars, power plants, industrial boilers, refineries, chemical plants, and others.

Because ozone formation needs sunlight and high temperature, high (and unhealthy) ozone concentrations are observed most commonly during the summer months, downwind of major precursor emissions sources, i.e., near urban environments. However, ozone can also be transported by the wind over long distances, eventually impacting both urban and rural areas.

Ozone is a highly reactive gas that is consumed by reactive processes on reaching the first interface in the lung, the lung lining fluid compartment. Reactions between ozone and antioxidants tend to dominate in this compartment, during the body's attempt to protect itself.

But when ozone reacts with other substrates in lung lining fluid, such as protein or lipid, damage occurs, eating away at the lung, and secondary oxidation products arise that transmit toxic signaling to the underlying pulmonary epithelium. These secondary oxidation products arising from ozone initiate a number of cellular responses, including cytokine generation, adhesion molecule expression, and tight junction modification. Together, these responses lead to the influx of inflammatory cells to the lung. Moreover, lung permeability is increased and edema (or fluid in the lung) develops. Because inhaled oxidants initiate these pathologic processes they can then contribute to the pathogenesis and/or exacerbation of ozone induced disease.

My colleague, Dr. Atanu Sarkar, will further discuss the public health implications of ozone's impacts on human health shortly. However, ozone exposure does not only impact human health, but it also affects vegetation and ecosystems, such as forests, parks, wildlife refuges and wilderness areas. Ozone specifically harms vegetation during the growing system, by reducing photosynthesis, slowing the growth of the plants, and increasing the plants' sensitivity to disease.

Because of its impacts on human health and ecosystems, ozone is one of the criteria pollutants for which the US Environmental Protection Agency sets national ambient air quality standards. Currently, the primary and secondary standard for ozone is 70 parts per billion for the daily maximum 8-hour concentration. Next, my colleagues will present strong evidence in opposition to the current Administration's proposed rule to retain, without revision, this standard. We urge that a lower ozone standard is implemented.

Thank you for your attendance.

Speaker 2: Dr.Atanu Sarkar
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How does Ozone affect the human health?

As Marianthi said *Ozone: Good high up and bad nearby.*
'Ground level' or 'tropospheric' or 'bad' ozone in the air we breathe can cause inflammation and damage to the airway lining and thus it has been compared to the skin inflammation caused by sunburn [1,2].

Since ground level ozone is formed in presence of heat and sunlight, on hot sunny days it can reach unhealthy levels. Even relatively low levels of ozone can cause health effects. Breathing ozone can trigger a variety of health problems including chest pain, coughing, throat irritation, and airway inflammation. It can also reduce lung function and harm lung tissue. When people inhale ozone, it causes constriction of the airway muscle, traps air in the alveoli leading to wheezing and shortness of breath and thus makes it more difficult to breathe deeply and vigorously. The exposed people complain about pain when taking a deep breath, coughing and sore or scratchy throat. Eventually, inhalation of ozone makes the lungs more susceptible to infection [2,3].

People most at risk from breathing air containing ozone include people with pre-existing medical conditions such as asthma, chronic bronchitis, emphysema and its exposure can trigger medical emergency. Children, older adults, and people who are active in outdoors, especially outdoor workers are vulnerable. In addition, people with certain genetic characteristics, and people with reduced intake of certain nutrients, such as vitamins C and E, are at greater risk from ozone exposure. It is important to note that children are at greatest risk from exposure to ozone because their lungs are still developing and they are more likely to be active outdoors when ozone levels are high, which increases their exposure. Children are also more likely than adults to have asthma (also known as childhood asthma) [2,3].

Epidemiological studies indicate that the rates of asthma attacks and medication usage increase on days with higher ozone concentrations. The rates of visits to hospital emergency rooms and hospital admissions for asthma and other respiratory conditions are also increased on such days. Multiple studies have found associations between short-term ozone exposures and total non-accidental mortality, which includes deaths from respiratory causes [4]. It has been estimated that some 21, 000 premature deaths per year are associated with ozone exceeding 70 $\mu g/m^3$ measured as a maximum daily 8-hour average in 25 EU countries [5]. In the US, a Global Burden of Disease study has estimated that some 7,000 extra deaths occur each year in our nation from Chronic Obstructive Disease (COPD) as a result of ambient ozone exposures [6].

Long-term chronic exposures to ozone have also been linked to permanent cumulative lung damage, including inhibited lung development in children and increased risk of death from respiratory causes among adults [2,3].

In addition, according to US department of agriculture, ground-level ozone causes more damage to plants than all other air pollutants combined, and therefore it affects our nation's food security [7]. The effects of ozone on individual plants can then have negative impacts on ecosystems, including loss of species diversity (less variety of plants, animals, insects, and fish), changes to habitat quality and water and nutrient cycles. Thus, ground level ozone can affect both human and ecosystem health [8].

Thank you for your attendance.

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Speaker 3: Dr. Kelvin Fong
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Human Health Effects of Ozone at Low Levels

The current ground-level ozone standard at 70 parts per billion (ppb) does not sufficiently protect the public health of Americans, as required by the Clean Air Act. A lower standard, as EPA's own reports have shown, would lead to fewer deaths and morbidities.

In 2015, when the EPA last revised the Ozone National Ambient Air Quality Standards (NAAQS), the Regulatory Impact Analysis found that reducing to 65 ppb would save 400 to 650 lives per year, accounting only for short-term effects of ozone [1]. When additionally accounting for long-term ozone exposure effects on mortality, a standard of 65 ppb could save another 1,500 lives per year (Table 6-20, page 6-79 in [1]). Moreover, a lower 65 ppb ozone standard would also result in reductions in fine particulate air pollution, or $PM_{2.5}$, that would not otherwise happen, avoiding another 900 to 2,000 US deaths per year (Table 6-22, page 6-81 in [1]). Clearly, the EPA's own calculations have shown that lowering the ozone standard below 70 ppb can avoid the loss of a large number of American lives every year.

A reduction in mortality with a lower ozone standard is supported by numerous articles in peer-reviewed scientific journals. With the American Cancer Society's Cancer Prevention II cohort, researchers found that a statistically significant positive association between ozone and all-cause mortality with a 10 ppb increase in ozone producing a 2% increase in all-cause mortality and a 3% increase in cardiovascular mortality in models that were adjusted for other ambient pollutants such as $PM_{2.5}$ and nitrogen dioxide (NO_2) [2]. This study performed extensive sensitivity analyses showing no evidence that the ozone effects were confounded by individual or area-based measures of socio-economic status or of pollution modeling strategy. The size of these effects have been replicated in other study settings, such as in Canada [3], where a population representative cohort of 2.5 million adults reported that per 10 ppb increase in ozone and adjusted for $PM_{2.5}$ and NO_2, there was a 1.8% increase in all-cause mortality and 3.8%

increase in cardiovascular mortality. Other studies demonstrating the link between long-term exposure to ozone and health detriments have since been published [4-7]. Some recent studies have even applied causal modeling, which EPA claims have been lacking in epidemiology studies [5, 8, 9]. A study using Medicare data found that there was a causal effect of ozone on all-cause mortality at levels as low as 32 ppb[9].

In the most recent Integrated Science Assessment for Ozone and Related Photochemical Oxidants [10], published earlier this year in 2020, the EPA again concluded that an ozone standard lower than 70 ppb would benefit the health of Americans. In experimental chamber exposure studies, lung function in healthy adults continued to improve as ozone concentrations decreased to 60 ppb (page IS-1 in [10]). When looking at real-world evidence from epidemiologic studies, improved lung function was observed as ozone decreased down to as low as 33 ppb (page IS-25 in [10]). Overall, the 2020 Integrated Science Assessment concluded that ozone causally and negatively affects the human respiratory system (page IS-7 in [10]), reaffirming what was already known in 2015 but with even more substantial scientific evidence. The report concluded that there is strong evidence that ozone exposure leads to increased hospital admissions, as well as emergency department visits related to respiratory conditions, which include asthma and chronic obstructive pulmonary disease.

In fact, there has been mounting evidence that ozone negatively affects vital bodily functions. The aforementioned 2020 Integrated Science Assessment concluded that short-term exposure to ozone likely causes negative effects on the metabolic system (page IS-7 and Appendix 5 in [10]). Ozone exposure is also associated with impaired insulin tolerance and elevated fasting glucose levels, which are tell-tale symptoms of metabolic syndrome and diabetes [11]. For over 27 million Americans with diabetes, especially those who are most at-risk, ozone exposure makes their lives more difficult to manage, reducing their quality of life. Epidemiologic studies have found that there is an increased risk of diabetes or metabolic syndrome at ozone concentrations below 30 ppb, which is less than half of the current and proposed standard [12] (cited on page 5-31 in [10]).

Given the totality of the latest evidence, the decision to retain the ozone standard at 70 ppb will not adequately protect health of Americans. We are lagging behind countries around the world that have already acted responsibly to adjust their ozone standards to below 70 ppb. Canada, our neighbor and ally, sets its standard at 62 ppb (the 3-year average of the annual 4th highest daily maximum 8-hour average) [13].

The EPA must recognize its responsibility to protect the health of Americans and withdraw its decision to retain the ozone standard at 70 ppb. A lower ozone standard is supported by current scientific evidence and will protect the health of millions of Americans, especially those most who are most vulnerable.

Thank you.

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Speaker 4: Dr. George D. Thurston
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Ozone Standard Setting Process Issues and ISEE NA Chapter Recommendations

The EPA's dereliction of its duty under the Clean Air Act on the ozone standard is part of a larger problem. The North American Chapter of the ISEE remains concerned about the litany of unwarranted changes the EPA has made to the Clean Air Scientific Advisory Committee (CASAC) and the NAAQS review process. The myriad of changes to the NAAQS review process are collectively harmful to the quality, credibility, and integrity of the scientific review process and to the CASAC as an advisory body. The current CASAC is unqualified to interpret epidemiologic studies, given that it lacks adequate depth and diversity of epidemiologic expertise.

In this case, CASAC's Ozone Panel was inappropriately disbanded in October 2018. This panel normally comprises a set of appropriate experts from diverse scientific disciplines, including epidemiology, toxicology, and human clinical studies. As just discussed, the available scientific data provide clear and compelling evidence that the current ozone standards are not adequate to sufficiently protect human health, and that EPA has ignored the "best available science".

While past implementation of the current Ozone NAAQS undoubtedly has reduced the burden of disease associated with air pollution exposures, there is still significant need for improvement. The Global Burden of Disease Study has estimated that thousands of Americans needlessly die each year from exposure to ozone air pollution exposure at current levels. Clearly, the longer the EPA delays taking action on lowering this ozone standard, these health damages will continue.

We strongly oppose an EPA decision to retain the current ozone NAAQS standard. This decision is clearly contrary to the state of the science, which demonstrates that adverse health effects are experienced below 70ppb and, hence, that the Administrators' decision violates the Clean Air Act requirement to use the "best available science" and to set standards "to protect public health with an adequate margin of safety." The EPA proposal does neither. ISEE endorses the setting of a lower standard that would be consistent with the current state of the science and

the Clean Air Act. For example, lowering the annual standard from 70 to 60 ppb, as recommended by the American Thoracic Society, would substantially lower O_3 pollution in the US, and would, upon achieving compliance, successfully avoid many thousands of needless deaths, hospital admissions, and other adverse health effects that occur each year from ozone air pollution.

Thank you. I hope you take our comments to heart.