Comments of the American Lung Association on EPA's Second Draft Risk and Exposure Assessment and Second Draft Policy Assessment on the Review of the National Ambient Air Quality Standards for Ozone

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SUMMARY

Based on the evidence available in these assessments, CASAC should recommend to EPA a much stronger range for the primary ozone standard than the outdated default range of 60 to 70 ppb that was under consideration nine years ago before this latest science assessment was completed. The new evidence indicates that a range of 55-60 ppb is needed to protect public health.

In this review, the evidence is stronger for most every health endpoint, with causal findings strengthened from "suggestive" to "likely causal" for cardiovascular effects and total mortality from short-term exposures, and for respiratory effects from long-term exposures. This stronger evidence necessitates greater public health protection.

There are twice as many controlled human exposure studies available in this review. These studies show lung function decrements at 60 ppb in healthy young adults, including a new study showing inflammation at 60 ppb. Inflammation is clearly an adverse effect, especially in asthmatics, and a ten percent decline in lung function is considered adverse for people with respiratory conditions whose breathing is already impaired. A primary standard below 60 ppb is needed to protect children, the elderly, and people with asthma.

Community health studies in Europe and North America have demonstrated consistent, positive relationships between ozone air pollution and hospital admissions and emergency department visits for respiratory causes at mean 8-hour maximum ozone concentrations less than 60 ppb.

Additionally, the draft Policy Assessment makes abundantly clear that the current standard is not protective of public health and should not be retained.

THE URGENT NEED FOR ACTION

Ozone is one of the most pervasive and pernicious of the common air pollutants. Ozone is a powerful oxidant, so powerful that it is used to treat and disinfect drinking water supplies. At ambient concentrations, ozone has been shown to cause

a variety of harms: rotting out rubber tires; damaging forests and crops; and endangering human health.

Ozone enters the human body via the lungs, and that is where the most damage occurs. Respiratory harms range from impeding inspiration to causing inflammation, coughing, and increased susceptibility to colds and flu. Ozone exacerbates asthma, leading to increased reliance on medication and increased visits to hospital emergency departments. There is now strong evidence that ozone increases the risk of premature death.

The long-term effects of ozone are also well documented. When infant monkeys are exposed to high concentrations of ozone, their lung development is stunted. Similarly, children growing up in more polluted areas never develop the lung capacity of their peers raised in less polluted environments.

Advances in biostatistics have enabled epidemiologists to tease out the effects of ozone from that of other air pollutants and confounding factors. We now know that ozone contributes to a range of public health harms including respiratory and cardiac effects, and even premature death, at concentrations well below the current standards.

The Clean Air Act requires EPA to set National Ambient Air Quality Standards (NAAQS) that protect the public health, including the health of sensitive populations, with an adequate margin of safety. The Act requires EPA to review the standards every five years, in light of advancements in the science, to ensure that the standards are health-protective.

The fact that the current standard is not protective of public health is well established, and has been for many years. That was the conclusion of EPA during the reconsideration process, with full concurrence by the Clean Air Scientific Advisory Committee (CASAC).

We strongly concur with the conclusion of the second draft Policy Assessment that the current standard is not protective of public health, based on the results of the *Integrated Science Assessment* and the *Risk and Exposure Assessment*.

STRIKING FINDINGS FROM THE INTEGRATED SCIENCE ASSESSMENT

The evidence base for ozone is stronger than for any other air pollutant. There are strong lines of evidence from all three major scientific disciplines: toxicology, epidemiology, and controlled human exposure studies.

<u>60 to 70 ppb Should Not be the Default Range for the Standard</u>

Much has changed since EPA last revised the ozone standard in March 2008. In September 2008, EPA initiated the current review of the standard with a call for

new information. EPA assessed hundreds of new scientific studies in the course of the review.

The Agency issued three draft *Integrated Science Assessments (ISAs)* that were thoroughly reviewed and vetted by CASAC. The final assessment, issued in early 2013 is based on a much larger evidence base than was available in 2006, when EPA completed the *Criteria Document* in the last review of the ozone standard.

Based upon the substantial new information available, the 2013 ISA reached much stronger conclusions about the health effects of ozone than had been reached in the prior review. The criteria for evaluating studies and reaching causal determinations is carefully laid out in the ISA, and were thoroughly vetted by CASAC. Conclusions are reached based on multiple lines of evidence and multiple studies, demonstrating coherence, consistency, and plausibility.

Specifically, the 2013 ISA finds:

--a conclusive determination that ozone causes adverse respiratory effects;

-- several additional controlled human exposure studies demonstrating respiratory deficits and inflammation in healthy young adults at **60 ppb**.;

-- stronger findings that the adverse effect of ozone on cardiovascular health are likely causal;

-- new information suggesting reproductive effects, such as increased risk of low birth weight babies;

-- new conclusions about suggestive neurological effects;

--new community health studies strengthening the link between ozone exposure and mortality, even at concentrations below the current standards; and

-- new information about the impact of longer-term exposures on respiratory health endpoints such as pulmonary inflammation and injury, and new onset asthma.

ISA Table 1-1 compares the causal findings from the 2013 ISA, with those of the 2006 *Criteria Document*.

Like the 2006 *Air Quality Criteria Document*, the 2013 ISA found there was a **causal relationship** between short-term exposure to ozone and **respiratory effects**.

For almost every other health outcome and exposure duration evaluated, the ISA **reached stronger causal determinations** in 2013 than in 2008.

For three critical health outcomes, scientific evidence in 2013 was so strong enough to indicate a "**likely causal relationship**:"

- **cardiovascular effects from short-term exposures**;
- **total mortality from short-term exposures**; and
- **respiratory effects from long-term exposures**.

Table 1-1 below, excerpted from the ISA, highlights those health outcomes for which the causal determination has been strengthened since the last review.[1]

Table 1-1 Summary of O_3 causal determinations by exposure duration and health outcome.

Health Outcome[a]	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Short-term Exposure to O_3		
Respiratory effects	The overall evidence supports a causal relationship between acute ambient O_3 exposures and increased respiratory morbidity outcomes.	Causal Relationship
Cardiovascular effects	The limited evidence is highly suggestive that O_3 directly and/or indirectly contributes to cardiovascular-related morbidity, but much remains to be done to more fully substantiate the association.	Likely to be a Causal Relationship
Central nervous system effects	Toxicological studies report that acute exposures to O_3 are associated with alterations in neurotransmitters, motor activity, short and long term memory, sleep patterns, and histological signs of neurodegeneration.	Suggestive of a Causal Relationship
Total Mortality	The evidence is highly suggestive that O_3 directly or indirectly contributes to non-accidental and cardiopulmonary-related mortality.	Likely to be a Causal Relationship
Long-term Exposure to O_3		
Respiratory effects	The current evidence is suggestive but inconclusive for respiratory health effects from long-term O_3 exposure.	Likely to be a Causal Relationship
Cardiovascular effects	No conclusions in the 2006 O_3 AQCD.	Suggestive of a Causal Relationship
Reproductive and developmental effects	Limited evidence for a relationship between air pollution and birth-related health outcomes, including mortality, premature births, low birth weights, and birth defects, with little evidence being found for O_3 effects.	Suggestive of a Causal Relationship
Central nervous system effects	Evidence regarding chronic exposure and neurobehavioral effects was not available.	Suggestive of a Causal Relationship
Cancer	Little evidence for a relationship between chronic O_3 exposure and increased risk of lung cancer.	Inadequate to Infer a Causal Relationship
Total Mortality	There is little evidence to suggest a causal relationship between chronic O_3 exposure and increased risk for mortality in humans.	Suggestive of a Causal Relationship

[a]Health effects (e.g., respiratory effects, cardiovascular effects) include a spectrum of outcomes, from measureable subclinical effects (e.g., blood pressure), to more obvious effects (e.g., medication use, hospital admissions), and cause-specific mortality. Total mortality includes all-cause (non-accidental) mortality, as well as cause-specific mortality (e.g., deaths due to heart attacks).

Several other types of health effects are newly classified as **suggestive of a causal relationship**, by the 2013 ISA:

- **central nervous system** effects from short-term exposures;
- **cardiovascular effects** from long-term exposures;

[1]2013 ISA, pp 2-23.

- **neurological effects** from long-term exposure; and
- **total mortality** from long-term exposure.

The point is that there is considerably more certainty than in the last review for several critical health endpoints. In that EPA sometimes cites "uncertainty" in support of a standard at the upper end of the range, the uncertainty regarding numerous key health effects has been substantially reduced in this review. That should factor into a development of a more protective range than has previously been considered.

Under the Clean Air Act, EPA is obliged to set air quality standards that protect public health from proven, as well as anticipated health effects.

Revisions to the standards must reflect the increased strength of the evidence, and the breadth of adverse health effects now attributable to ozone air pollution.

In the last review and during the reconsideration process, the American Lung Association and other leading medical organizations including the American Academy of Pediatrics American Thoracic Society, American Medical Association, American College of Chest Physicians, American College of Preventive Medicine, American College of Occupational and Environmental Medicine, American Association of Cardiovascular and Pulmonary Rehabilitation and National Association for the Medical Direction of Respiratory Care supported an 8-hour average standard of 60 ppb or below, based on strong evidence from the controlled human exposure studies and the epidemiological studies.[2]

Given the strength and extent of the new evidence, it is apparent that a standard of 70 ppb, at the upper end of the range in the *second draft Policy Assessment*, should no longer be under consideration, given the causal findings in the ISA.

ISA CONCLUSIONS ON HEALTH EFFECTS

Beyond the causal findings, the ISA presents an integrated assessment of the new science, and evaluates it in the context of earlier evidence.

Chapter 2 of the document, *the Integrative Summary*, presents clear conclusions about the concentrations at which adverse health effects are experienced.

Table 2-1 summarizes the specific conclusions of the ISA for specific health effects, as compared to the conclusions from the 2006 *Criteria Document*.

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[2] Comments of American Lung Association, Environmental Defense, Sierra Club, on the Proposed Revisions to the National Ambient Air Quality Standards for Ozone, October 9, 2007.

For a number of important respiratory health endpoints, including lung function decrements, inflammation, hospital and emergency department visits for respiratory causes, the ISA indicates adverse effects at 60 ppb. This provides strong support for an upper end of the range no higher than 60 ppb.

According to the *Integrated Science Assessment* issued in February 2013:

Short-term Exposures

-- Several studies of healthy young adults have demonstrated a reduction in lung function at concentrations of **60 ppb**. Some individuals respond more severely than the group average.

-- Lung function declines are especially of concern to children and adults with asthma and COPD, because these individuals have reduced pulmonary reserves.

-- Because healthy adults are harmed at **60 ppb,** the standards must be set lower to protect sensitive populations --such as children, children with asthma, and people who work or exercise outdoors -- with an adequate margin of safety.

-- Increases in airway responsiveness, a hallmark of asthma, have been well-demonstrated in young, healthy adults at **80 ppb**, and in laboratory rats at **50 ppb**.

-- Epidemiologic studies with mean 8-hour maximum concentrations **below 73 ppb** provide new evidence for associations between ambient ozone exposure and pulmonary injury and oxidative stress.

-- Controlled human exposure studies have demonstrated inflammatory responses at **60 ppb**. Inflammation of the lining of the lungs is a serous health concern.

-- Children with asthma face an increase in respiratory symptoms such as coughing, wheezing, and shortness of breath at mean 8-hour maximum ozone concentrations less than **69 ppb**.

--Short-term concentrations as low as **80 ppb** repress immune function, increasing susceptibility to respiratory infections such as influenza.

-- Concentrations as low as **80 ppb** are associated with enhanced allergic responses in asthmatics, and at **200 ppb** in test rodents.

-- Community health studies in Europe and North America have demonstrated consistent, positive associations between ozone air pollution and hospital admissions and emergency department visits for respiratory causes. Generally, mean 8-hour maximum ozone concentrations were less than **60 ppb**.

-- Consistently positive associations between ozone and respiratory mortality have been reported in single-city and multi-city studies. The mean 8-hour maximum ozone concentration in these studies is less than **63 ppb**.

-- Studies of ozone and **mortality** have not identified a threshold below which there are no effects.

Long-Term Exposures

Longer-term studies have also demonstrated the need for a stricter standard to protect against **chronic effects.**

-- There is increased evidence that chronic exposure to ozone may increase the risk of new onset asthma, at mean annual 8-hour maximum concentrations of **55.2 ppb**. Among active children, those living in more polluted areas run a greater risk of developing asthma.

--Studies with mean annual 8-hour maximum ozone concentrations less than **41 ppb** have found that chronic ozone exposures puts kids with asthma at greater risk of a hospital admission.

--Several new epidemiologic studies link ozone exposures of **69 ppb** (mean 8-hour maximum concentration) to inflammation and injury to the lung tissue.

Below, we have highlighted the key conclusions in the 2013 ISA that go beyond those in the 1996 *Criteria Document* in Table 2-1 from the ISA.[3]

[3] 2013 ISA pp. 2-20 to 2-24.

Table 2-1 Summary of evidence from epidemiologic, controlled human exposure, and animal toxicological studies on the health effects associated with short- and long-term exposure to O_3.

Health Outcome	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Short-Term Exposure to O_3		
Respiratory effects	The overall evidence supports a causal relationship between acute ambient O_3 exposures and increased respiratory morbidity outcomes.	Evidence integrated across controlled human exposure, epidemiologic, and toxicological studies and across the spectrum of respiratory health endpoints continues to demonstrate that there **is a causal relationship between short-term O_3 exposure and respiratory health effects.**
Lung function	Results from controlled human exposure studies and animal toxicological studies provide clear evidence of causality for the associations observed between acute (≤ 24 h) O_3 exposure and relatively small, but statistically significant declines in lung function observed in numerous recent epidemiologic studies. Declines in lung function are particularly noted in children, asthmatics, and adults who work or exercise outdoors.	Recent controlled human exposure studies demonstrate group mean decreases in FEV_1 in the range of 2 to 3% with 6.6 hour exposures to as low as **60 ppb** O_3. The collective body of epidemiologic evidence demonstrates associations between short-term ambient O_3 exposure and decrements in lung function, particularly in children with asthma, children, and adults who work or exercise outdoors.
Airway hyperresponsiveness	Evidence from human clinical and animal toxicological studies clearly indicate that acute exposure to O_3 can induce airway hyperreactivity, thus likely placing atopic asthmatics at greater risk for more prolonged bouts of breathing difficulties due to airway constriction in response to various airborne allergens or other triggering stimuli.	A limited number of studies have observed airway hyperresponsiveness in rodents and guinea pigs after exposure to less than **300 ppb** O_3. As previously reported in the 2006 O_3 AQCD, increased airway responsiveness has been demonstrated at **80 ppb** in young, healthy adults, and at **50 ppb** in certain strains of rats.

Health Outcome	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Pulmonary inflammation, injury and oxidative stress	The extensive human clinical and animal toxicological evidence, together with the limited available epidemiologic evidence, is clearly indicative of a causal role for O_3 in inflammatory responses in the airways.	Epidemiologic studies provided new evidence for associations of ambient O_3 with mediators of airway inflammation and oxidative stress and indicate that higher antioxidant levels may reduce pulmonary inflammation associated with O_3 exposure. Generally, these studies had mean 8-h max O_3 concentrations less than **73 ppb**. Recent controlled human exposure studies show O_3-induced inflammatory responses at 60 ppb, the lowest concentration evaluated.
Respiratory symptoms and medication use	Young healthy adult subjects exposed in clinical studies to O_3 concentrations ≥ 80 ppb for 6 to 8 h during moderate exercise exhibit symptoms of cough and pain on deep inspiration. The epidemiologic evidence shows significant associations between acute exposure to ambient O_3 and increases in a wide variety of respiratory symptoms (e.g., cough, wheeze, production of phlegm, and shortness of breath) and medication use in asthmatic children.	The collective body of epidemiologic evidence demonstrates positive associations between short-term exposure to ambient O_3 and respiratory symptoms (e.g., cough, wheeze, and shortness of breath) in children with asthma. Generally, these studies had mean 8-h max O_3 concentrations less than **69 ppb**.
Lung host defenses	Toxicological studies provided extensive evidence that acute O_3 exposures as low as 80 to 500 ppb can cause increases in susceptibility to infectious diseases due to modulation of lung host defenses. A single controlled human exposure study found decrements in the ability of alveolar macrophages to phagocytize microorganisms upon exposure to 80 to 100 ppb O_3.	Recent controlled human exposure studies demonstrate the increased expression of cell surface markers and alterations in sputum leukocyte markers related to innate adaptive immunity with short-term O_3 exposures of **80-400 ppb**. Recent studies demonstrating altered immune responses and natural killer cell function build on prior evidence that O_3 can affect multiple aspects of innate and acquired immunity with short-term O_3 exposures as low as **80 ppb**.
Allergic and asthma related responses	Previous toxicological evidence indicated that O_3 exposure skews immune responses toward an allergic phenotype, and enhances the development and severity of asthma-related responses such as AHR.	Recent controlled human exposure studies demonstrate enhanced allergic cytokine production in atopic individuals and asthmatics, increased IgE receptors in atopic asthmatics, and enhanced markers of innate immunity and antigen presentation in health subjects or atopic asthmatics with short-term exposure to **80-400 ppb** O_3, all of which may enhance allergy and/or asthma. Further evidence for O_3-induced allergic skewing is provided by a few recent studies in rodents using exposure concentrations as low as **200 ppb**.

Health Outcome	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Respiratory Hospital admissions, ED visits, and physician visits	Aggregate population time-series studies observed that ambient O_3 concentrations are positively and robustly associated with respiratory-related hospitalizations and asthma ED visits during the warm season.	Consistent, positive associations of ambient O_3 with respiratory hospital admissions and ED visits in the U.S., Europe, and Canada with supporting evidence from single city studies. Generally, these studies had mean 8-h max O_3 concentrations less than **60 ppb**.
Respiratory Mortality	Aggregate population time-series studies specifically examining mortality from respiratory causes were limited in number and showed inconsistent associations between acute exposure to ambient O_3 exposure and respiratory mortality.	Recent multicity time-series studies and a multicontinent study consistently demonstrated associations between ambient O_3 and respiratory-related mortality visits across the U.S., Europe, and Canada with supporting evidence from single city studies. Generally, these studies had mean 8-h max O_3 concentrations less than **63 ppb.**
Cardiovascular effects	The limited evidence is highly suggestive that O_3 directly and/or indirectly contributes to cardiovascular-related morbidity, but much remains to be done to more fully substantiate the association.	The overall body of evidence across disciplines indicates that there **is likely to be a causal relationship for short-term exposures to O_3 and cardiovascular effects.**
Central nervous system effects	Toxicological studies report that acute exposures to O_3 are associated with alterations in neurotransmitters, motor activity, short- and long-term memory, sleep patterns, and histological signs of neurodegeneration.	Together the evidence from studies of short-term exposure to O_3 **is suggestive of a causal relationship between O_3 exposure and CNS effects.**
Total Mortality	The evidence is highly suggestive that O_3 directly or indirectly contributes to non-accidental and cardiopulmonary-related mortality.	Taken together, the body of evidence indicates that there **is likely to be a causal relationship between short-term exposures to O_3 and total mortality.**
Long-term Exposure to O_3		
Respiratory effects	The current evidence is suggestive but inconclusive for respiratory health effects from long-term O_3 exposure.	Recent epidemiologic evidence, combined with toxicological studies in rodents and non-human primates, provides biologically plausible evidence that there **is likely to be a causal relationship between long-term exposure to O_3 and respiratory health effects.**
New onset asthma	No studies examining this outcome were evaluated in the 2006 O_3 AQCD.	Evidence that different genetic variants (HMOX, GST, ARG), in combination with O_3 exposure, are related to new onset asthma. These associations were observed when subjects living in areas where the mean annual 8-h max O_3 concentration was **55.2 ppb**, compared to those who lived where it was **38.4 ppb**.

Health Outcome	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Asthma hospital admissions	No studies examining this outcome were evaluated in the 2006 O_3 AQCD.	Chronic O_3 exposure was related to first childhood asthma hospital admissions in a positive concentration-response relationship. Generally, these studies had mean annual 8-h max O_3 concentrations less than **41 ppb**.
Pulmonary structure and function	Epidemiologic studies observed that reduced lung function growth in children was associated with seasonal exposure to O_3; however, cohort studies of annual or multiyear O_3 exposure observed little clear evidence for impacts of longer-term, relatively low-level O_3 exposure on lung function development in children. Animal toxicological studies reported chronic O_3-induced structural alterations, some of which were irreversible, in several regions of the respiratory tract including the centriacinar region. Morphologic evidence from studies using exposure regimens that mimic seasonal exposure patterns report increased lung injury compared to conventional chronic stable exposures.	Evidence for pulmonary function effects is inconclusive, with some new epidemiologic studies observing positive associations (mean annual 8-h max O_3 concentrations less than **65 ppb**). Information from toxicological studies indicates that long-term exposure during development among infant monkeys (**500 ppb**) and adult rodents (**>120 ppb**) can result in irreversible morphological changes in the lung, which in turn can influence pulmonary function.
Pulmonary inflammation, injury and oxidative stress	Extensive human clinical and animal toxicological evidence, together with limited epidemiologic evidence available, suggests a causal role for O_3 in inflammatory responses in the airways.	Several epidemiologic studies (mean 8-h max O_3 concentrations less than **69 ppb**) and toxicology studies (as low as **500 ppb**) add to observations of O_3-induced inflammation and injury.
Lung host defenses	Toxicological studies provided evidence that chronic O_3 exposure as low as 100 ppb can cause increases in susceptibility to infectious diseases due to modulation of lung host defenses, but do not cause greater effects on infectivity than short exposures.	Consistent with decrements in host defenses observed in rodents exposed to **100 ppb** O_3, recent evidence demonstrates a decreased ability to respond to pathogenic signals in infant monkeys exposed to **500 ppb** O_3.
Allergic responses	Limited epidemiologic evidence supported an association between ambient O_3 and allergic symptoms. Little if any information was available from toxicological studies.	Evidence relates positive outcomes of allergic response and O_3 exposure but with variable strength for the effect estimates; exposure to O_3 may increase total IgE in adult asthmatics. Allergic indicators in monkeys were increased by exposure to O_3 concentrations of **500 ppb**.
Respiratory mortality	Studies of cardio-pulmonary mortality were insufficient to suggest a causal relationship between chronic O_3 exposure and increased risk for mortality in humans.	A single study demonstrated that exposure to O_3 (long-term mean O_3 less than **104 ppb**) elevated the risk of death from respiratory causes and this effect was robust to the inclusion of $PM_{2.5}$.

Health Outcome	Conclusions from 2006 O_3 AQCD	Conclusions from this ISA
Cardiovascular Effects	No studies examining this outcome were evaluated in the 2006 O_3 AQCD.	The overall body of evidence across disciplines **is suggestive of a causal relationship for long-term exposures to O_3 and cardiovascular effects.**
Reproductive and developmental effects	Limited evidence for a relationship between air pollution and birth-related health outcomes, including mortality, premature births, low birth weights, and birth defects, with little evidence being found for O_3 effects.	Overall, the evidence **is suggestive of a causal relationship between long-term exposures to O_3 and reproductive and developmental effects.**
Central nervous system effects	Toxicological studies reported that acute exposures to O_3 are associated with alterations in neurotransmitters, motor activity, short and long term memory, sleep patterns, and histological signs of neurodegeneration. Evidence regarding chronic exposure and neurobehavioral effects was not available.	Together the evidence from studies of long-term exposure to O_3 **is suggestive of a causal relationship between O_3 exposure and CNS effects.**
Cancer	Little evidence for a relationship between chronic O_3 exposure and increased risk of lung cancer.	Overall, the evidence **is inadequate to determine if a causal relationship exists between ambient O_3 exposures and cancer.**
Total Mortality	There is little evidence to suggest a causal relationship between chronic O_3 exposure and increased risk for mortality in humans.	Collectively, the evidence **is suggestive of a causal relationship between long-term O_3 exposures and total mortality.**

These strong, new conclusions should be carried forward more forcefully in the Policy Assessment.

Sensitive Populations Must be Protected

The ISA identifies several subpopulations that are particularly vulnerable to the effects of ozone air pollution. These groups include children, the elderly, and people with respiratory conditions such as asthma. In addition, people who work or exercise outdoors are at increased risk due to their increased exposure to ozone.

We would add that there is growing information on obesity as a potential risk factor for increased susceptibility to ozone air pollution. Two-thirds of the U.S. population is classified as overweight or obese, including a growing number of children and adolescents. Obese individuals have higher breathing rates, which can increase their exposure to ozone and other air pollutants.[4][5]

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[4] Koman, PD. How Does the Obesity Epidemic Affect Risk from Air Pollution? Risk Science Center Occasional Papers 1:2012, University of Michigan School of Public Health, 12-1 - 2012. http://www.sph.umich.edu/riskcenter/occasionalpaper/rsckomanpaper.pdf

[5] Pierre Brochu, Michèle Bouchard, Sami Haddad. Physiological Daily Inhalation Rates for Health Risk Assessment in Overweight/Obese Children, Adults, and Elderly. *Risk Analysis*, 22 October 2013. DOI: 10.1111/risa.12125.

Under the Clean Air Act, the NAAQS must protect these sensitive populations with an adequate margin of safety. It follows that standards must be set below the levels shown to cause harm in healthy test subjects.

The Mean Concentrations Do Not Tell the Whole Story

The mean concentrations reported in the table above, and commonly reported as a summary statistic, do not tell the whole story. That is because adverse effects are occurring along a continuum of ozone concentrations.

In considering the results reported for epidemiological studies, EPA has to look at the distribution of air quality values.

Adverse effects are occurring at concentrations both above and below the mean. The bulk of the effects occur within one standard deviation of the mean.

One standard deviation below the mean in the most relevant statistic to consider for standard setting purposes, because it reflects the concentration level above which the majority of adverse health effects occur.

The draft *Policy Assessment* takes a reductionist approach to the evaluation of the epidemiologic literature, choosing to focus on North American multi-city studies to the exclusion of other studies. The *Assessment* further restricts its consideration of the epidemiologic studies by focusing on those study locations that would have met the current standard or various alternative standards.

Even using that narrowed focus, the *Policy Assessment* provides sufficient evidence to show the need for a stronger range than originally drafted.

THE ROLE OF SAFETY FACTORS

Occupational and environmental standard setting entails interpreting evidence from a variety of disciplines such as toxicology, exposure studies, and epidemiology, and translating it into meaningful, health-protective limits.

To extrapolate laboratory toxicology data to threshold limits or standards, regulators routinely employ **safety factors, or uncertainty factors**. For instance, safety factors must account for **intra**-species variability, **inter**-species variability, and several other factors.

EPA has previously accounted for **six distinct uncertainty factors** in setting health-protective standards.[6] The descriptions below are taken from EPA's own language.

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[6] U.S. EPA Office of Pesticide Programs. Determination of the Appropriate FQPA Safety Factor in Tolerance Assessment. February 28, 2002. http://www.epa.gov/oppfead1/trac/science/determ.pdf

1) **Inter-species uncertainty factor,** intended to account for uncertainty in extrapolating animal data to humans;

2) **Intra-species uncertainty factor**, intended to account for the variation in sensitivity among members of the human population, including children;

3) **An uncertainty factor to extrapolate from subchronic to chronic data**, if deriving a chronic reference dose.

4) **An uncertainty factor to extrapolate from a LOEAL (lowest observed adverse effect level) to a (surrogate) NOAEL(no observed adverse effect level),** if no appropriate NOEAL can be detected from the toxicology database.

5) **Database uncertainty factor**, to account for absence of key data

6) **Modifying factor**, to account for other database limitations such as small sample size or poor exposure dose.

Typically, a **factor of ten** is applied to account for the interspecies uncertainty factor, and **another factor of ten** for the intraspecies uncertainty factor. Variable factors may be used to address the other sources of uncertainty.

In the air quality standards arena, however, the *draft Policy Assessment* does not discuss the use of safety or uncertainty factors in the interpretation of the scientific record. Nonetheless, such factors can be used in providing advice to EPA on the primary standard.

Apply a Safety Factor to Concentrations in Controlled Human Exposure Studies

It is certainly appropriate to consider use of a safety factor in interpreting the results of the controlled human exposure studies for standard-setting purposes. These "chamber studies" most commonly employ healthy young adult volunteers. Since the standards must be set to protect infants, children, people with asthma, the elderly, and other sensitive populations, the exposure concentrations reported in the chamber studies must be adjusted *downward* when setting NAAQS.

The "rule of thumb" factor of ten may or may not be the appropriate safety factor in this context; but some safety or uncertainty factor is certainly needed to account for the differences between children and adults, healthy vs. unhealthy, and ozone responders, vs. the general population.

Apply Safety Factors to Concentrations in Toxicology Studies

Furthermore, the results of toxicology studies should have bearing on the recommended ranges for the standards. Some of the most innovative research on the health effects of ozone has been conducted on laboratory animals. For reasons

of economy, these studies are often conducted at high dosages. This enables effects to be detected with a small number of test subjects.

Toxicology studies can inform setting of air quality standards just as they are used to set water quality standards or pesticide tolerances. These studies should not be dismissed as irrelevant to selecting the level of the standard because they were conducted at higher than ambient concentrations. Rather, the safety factor concept is relevant to enable consideration of toxicology results in standard-setting.

The Policy Assessment Minimizes the Epidemiological Study Findings

With respect to the epidemiology studies, the question is which concentration level is relevant to standard-setting. Health effects reported for general population exposures may not be fully representative of effects in highly exposed populations. In past reviews, EPA has often relied on the mean concentration statistic as a guidepost.

A safety factor was intrinsically incorporated by setting a more restrictive form of the standard. For example, a 4th highest daily max form is intended to curtail exceedances of the standard for all but the most polluted days each year. The mean concentration level reported in the epidemiological studies is used as a guideline to set a "maximum" concentration level, thus providing a built in safety factor.

However, in the second draft *Policy Assessment*, EPA deviates from this approach.

The *Policy Assessment* identifies North American epidemiological and panel studies reporting associations with morbidity or mortality that were performed in areas that would have met the current ozone standard during the study period. These studies are summarized in Tables 3-2 and 3-4 of the draft *Policy Assessment*.

We concur that these studies provide powerful evidence that the current ozone air quality standards are not protective of public health.

But in considering alternative standards, as in Table 4-1, using a metric that includes only those studies conducted in areas that would have "met the current standard" eliminates the safety factor derived from setting a standard with a stringent form intended to prevent exceedances of a certain level.

Past reviews, such as for the 1997 PM standards, have not interpreted studies in this manner. Indeed the "form" of the standard, which defines the number of exceedances, has in some sense been relied upon to provide a margin of safety.

EPA Needs to Incorporate a Safety Factor in Interpreting Studies

This review needs to reincorporate a safety or uncertainty factor, in translating the results of the epidemiological studies into air quality standards. Important

information can be gleaned from these studies about the distribution of ozone concentrations where the preponderance of adverse health effects occur, but not as the Policy Assessment discusses them.

The draft *Policy Assessment* uses an over-simplification to dismiss epidemiological studies from consideration because they were conducted in places that would violate the current standard.

By using focusing only on studies that would meet the current *level* of the standard, the *Policy Assessment* eliminates the safety factor that stemmed from the *form* of the standard intended to minimize exceedances of a mean concentration observed in the epidemiological studies.

As we discuss below, the epidemiological studies do not justify a range of 60 to 70 ppb and provide strong evidence that a more protective range of 55 to 60 ppb is needed to protect public health with an adequate margin of safety.

CONTROLLED HUMAN EXPOSURE EVIDENCE SUPPORTS A STANDARD NO HIGHER THAN 60 ppb

In evaluating these chamber studies, it is important to recognize that a substantial fraction of subjects in these studies exhibited particularly marked responses in lung function and symptoms. Standards must be set to protect the more sensitive subjects, not just to protect against responses evident in the group mean effects.

Post-1996, two controlled human exposure studies were conducted that evaluated the effect on lung function -- forced expiratory volume in one second (FEV_1) -- of various exposure regimes to concentrations of ozone of 80 ppb, 60 ppb and 40 ppb, for 6.6. hours.[7] These studies by Adams were funded by the American Petroleum Institute and were intended to address the effect of various exposure regimes on lung function responses to ozone.

The Adams (2002) study reports that "some sensitive subjects experience notable effects at 0.06 ppm." According to the *Policy Assessment*, this is based on the observation that 20 percent of the subjects exposed to 0.06 ppm ozone had a greater than 10 percent decrement in FEV_1 even though the group mean response was not statistically different from the filtered air response. In a study with a small number of subjects—the response of individual subjects is more important than the group mean response. This is particularly true for ozone exposure, where research has long recognized the variability in individual responses.

With ozone, it is well-established that some people are relatively insensitive, while other individuals—the so-called "responders"—experience enhanced responses. Because of the expense of a clinical chamber study, these studies use a small number of healthy subjects

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[7] Mudway IS, Kelly FJ. An Investigation of Inhaled Ozone Dose and the Magnitude of Airway Inflammation in Healthy Adults. *Am J Respir Crit Med* 2004; 169: 1089-1095.

and the inter-subject variability is less than for the general population. For that reason, these substantial individual responses likely represent an understatement of the impact on a broader population.

In the Adams (2006) study, even group mean FEV_1 responses during the 60 ppb ozone exposures diverge from filtered-air and 40 ppb ozone exposures.[8]

The Brown et al analysis presents a comparison of pre- to post- exposure effects using data from the Adams 2006 publication, which indicates a significant effect on FEV_1 of 60 ppb ozone compared to filtered air.[9]

Additionally, the Adams 2006 paper reported that total subjective symptom scores reached statistical significance (relative to pre-exposure) at 5.6 and 6.6 hours, with the triangular exposure scenario. The article states that the pain on deep inspiration values followed a similar pattern to total subjective symptom scores. The *Policy Assessment* reports that the evaluation of pre- to post-exposure effects on both total subjective symptoms and pain on deep inspiration are suggestive of significant respiratory symptom effects at 60 ppb ozone.

In the Kim et al. 2011 study of healthy adults, exposures to 60 ppb decrease lung function and induce inflammation of the airways and have been shown to be statistically significant.[10]

Adding to the findings of adverse effects below the current standard, new evidence from Schelegle et al. 2009 finds that at 70 ppb ozone, healthy adult subjects experience large decrements in lung function and respiratory symptoms.[11]

The CASAC has previously indicated that a 10 percent decrement in FEV_1 as observed in multiple studies can lead to respiratory symptoms, especially in individuals with pre-existing heart or lung disease, and are considered adverse for people with lung disease

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[8] Adams, WC. (2006a). Comparison of chamber 6.6-h exposures to 0.04-0.08 ppm ozone via square-wave and triangular profiles on pulmonary responses. Inhal Toxicol 18: 127-136. http://dx.doi.org/10.1080/08958370500306107

[9] Brown, JS; Bateson, TF; McDonnell, WF. (2008). Effects of exposure to 0.06 ppm ozone on FEV1 in humans: A secondary analysis of existing data. Environ Health Perspect 116: 1023-1026. http://dx.doi.org/10.1289/ehp.11396

[10] Kim, CS; Alexis, NE; Rappold, AG; Kehrl, H; Hazucha, MJ; Lay, JC; Schmitt, MT; Case, M; Devlin, RB; Peden, DB; Diaz-Sanchez, D. (2011). Lung function and inflammatory responses in healthy young adults exposed to 0.06 ppm ozone for 6.6 hours. Am J Respir Crit Care Med 183: 1215-1221. http://dx.doi.org/10.1164/rccm.201011-1813OC

[11] Schelegle, ES; Morales, CA; Walby, WF; Marion, S; Allen, RP. (2009). 6.6-hour inhalation of ozone concentrations from 60 to 87 parts per billion in healthy humans. Am J Respir Crit Care Med 180: 265-272. http://dx.doi.org/10.1164/rccm.200809-1484OC

under according to the guidelines of the American Thoracic Society.[12]

The lung function decrements and inflammation reported in healthy adults at 60 ppb are statistically significant and adverse.

Pulmonary inflammation provides a mechanism by which ozone can cause more serious effects such as asthma exacerbations.

As the *Policy Assessment* correctly indicates at pp 4-10:

> given the occurrence of airway inflammation following exposures to 60 ppb and higher, it may be reasonable to expect that inflammation would also occur following exposures to O_3 concentrations somewhat below 60 ppb.

Proper interpretation of these controlled human exposure studies leads to the inescapable conclusion that an ozone standard must be set at 60 ppb or below, such as 55 ppb, in order to protect public health with an ample margin of safety.

Additional Support for an Upper Limit of 60 ppb from the Controlled Human Exposure Studies

In addition to the special sensitivity of those with asthma, COPD, and other respiratory diseases, several additional factors suggest that the chamber studies justify a more stringent standard:

First, exposures in these studies were for 6.6 hours, not 8 hours.

Ozone harm clearly increases with the cumulative dose. A standard with a longer exposure time than the study period demands a lower level than that shown to induce adverse respiratory effects. In other words, if the study protocol is eliciting adverse effects at 80 ppb or 60 ppb after 6.6 hour exposures, a standard set for an 8-hour period must be lower than the level at which effects are observed because of the longer averaging time and greater accumulated dose of ozone.

Second, individuals tested in chamber studies are generally healthy, not people with severe respiratory diseases. By law, standards must be set at levels that will protect sensitive subpopulations *with an adequate margin of safety*.

Third, subjects in controlled exposure studies are adults, not infants or children, who experience greater exposures due to their higher breathing rates.

Fourth, the full range of human responses cannot be detected in studies with a small number of subjects.

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[12] Samet JM. Clean Air Scientific Advisory Committee (CASAC) Response to Charge Questions on the Reconsideration of the 2008 Ozone National Ambient Air Quality Standards. EPA-CASAC-11-004. March 30, 2011.

Asthmatics who already experience increased airway reactivity and inflammation may find their symptoms worsened or prolonged by exposure to ozone. In a study comparing airway inflammation and responsiveness to ozone in normal and asthmatic subjects. Balmes et al. (1997) reported that the ozone-induced increases in percentage of neutrophils and total protein concentration in bronchoalveolar lavage fluid were significantly greater for the asthmatic subjects than for the nonasthmatic subjects. These data suggest that the inflammatory response of the asthmatic lung may be more intense, indicating the need for tighter standards than proposed in order to protect the health of asthmatics.[13]

As the *Policy Assessment* states on p. 3-88, asthmatic children are more likely to experience larger and/or more serious effects than healthy adults.

In light of the evidence of adverse effects at 60 ppb, it is clear that this is the upper limit that should be under consideration for a revised standard.

EPIDEMIOLOGICAL EVIDENCE SUPPORTS A STANDARD NO HIGHER THAN 60 ppb

In the last review, we filed comments identifying twenty North American studies which reported positive, statistically significant results for various health endpoints, for which EPA derived 98th percentile 8-hour daily maximum concentrations of about 85 ppb or lower.[74]

The studies in Table 3 below, are drawn from Appendix 3B of the Staff Paper (2006).

The data demonstrate that even after taking a broader view of the air quality statistics than the study authors, and after looking at different air quality metrics, adverse health effects are observed at concentrations at and well below the current standards.

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[13] Balmes JR, Aris RM, Chen, LL, Scannell C, Tager IB, Finkbeiner W, Christian D, Kelly T, Hearne PQ, Ferrando R, Welch B. Effects of ozone on normal and potentially sensitive human subjects. Part I: Airway inflammation and responsiveness to ozone in normal and asthmatic subjects. *Res Rep Health Eff Inst.* 1997; 78: 1-37.

Study Endpoints	98th percentile 8-hr daily max (ppb)
Respiratory Symptoms	
Mortimer et al., 2002	64.3
Delfino et al., 2003	34.8
Ross et al., 2002	68.8
Lung Function Changes	
Mortimer et al., 2002	64.3
Naeher et al., 1999	74
Brauer et al., 1996	55
Emergency Department Visits: Respiratory Diseases	
Delfino et al., 1997	57.5
Wilson et al., 2005 (Portland)	85
Friedman et al., 2001	85.8
Emergency Department Visits: Cardiovascular Outcomes	
Rich et al., 2005	74

Hospital Admissions: Cardiovascular Diseases	
Koken et al., 2003	64.5
Hospital Admissions: Respiratory Diseases	
Delfino et al., 1994	69
Burnett et al., 1994	79
Burnett et al., 1997	62
Yang et al., 2003	42.7
Moolgavkar et al., 1997	83.2
Burnett et al., 2001	77.7
Burnett et al., 1999	68.4
Schwartz et al., 1994	82.8
Mortality:	
Ito et al.,1996	76
Vedal et al., 2003	53.3

Table 3: Ozone Epidemiological Studies Showing Effects at Low Concentrations: EPA Derived 98th Percentile Statistics Near or Below the Current Standard

Source: American Lung Association, 2007, Derived from Staff Paper Appendix 3B. Ozone Epidemiological Study Results: Summary of effect estimates and air quality data reported in studies, distribution statistics for 8-hr daily maximum ozone concentrations for the study period and location, and information about monitoring data used in the study.

A very large case-crossover study of Medicare recipients in of 36 U.S. cities evaluated the effect of ozone and PM_{10} on respiratory hospital admissions in the elderly over a 13-year period. The study found that the risk of daily hospital admissions for COPD and pneumonia increased with short-term increases in ozone concentrations during the warm season, but not during the cold season. Importantly, 8-hour mean warm season ozone concentrations in this study ranged from 15 ppb in Honolulu to 63 ppb in Los Angeles.[14] Concentrations in most cities in the 40-55 ppb range. This study provides powerful evidence for a standard of 0.060 ppm or below.

People may die from ozone exposure even when concentrations are well below the current standards. Bell and colleagues followed up on their 2004 multi-city study to estimate the exposure-response curve for ozone and risk of mortality and to evaluate whether a threshold exists below which there is no effect. They applied several statistical models to data on air pollution, weather, and mortality for 98 U.S. urban communities for the period 1987-2000. The results show that any threshold would exist at very low concentrations, far below current U.S. standards.

The authors concluded:

> "[O]ur nationwide study provides strong and consistent evidence that daily changes in ambient O_3 exposure are linked to premature mortality, even at very low pollution levels, including an idealized scenario of complete adherence to current O_3 regulations.

Importantly even when days exceeding 0.060 were excluded from the analysis, the mortality effect was little changed. The relationship between mortality and ozone was evident even on days when pollution levels were below the 0.06 ppm. The ozone and mortality results do not appear to be confounded by temperature or PM_{10}.[15]

<u>Effects Persist Even After Excluding Concentrations above a Certain Level</u>

We would like to emphasize a number of studies that excluded observations above a certain concentration and still found effects. This study design provides compelling evidence of associations evident at low concentrations, and is very pertinent to regulatory standard setting.

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[14] Medina-Ramón M, Zanobetti A, Schwartz J. The Effect of Ozone and PM_{10} on Hospital Admissions for Pneumonia and Chronic Obstructive Pulmonary Disease: A National Multicity Study. *American Journal of Epidemiology 2006*; 163: 579-588.

[15] Bell ML, Peng RD, McDermott A, Zeger SL, Samet JM, Dominici F. The Exposure-Response Curve for Ozone and Risk of Mortality and Adequacy of Current Ozone Regulations. *Environ Health Perspect* 2006; 114:532-536. Ozone and short-term mortality in 95 US urban communities, 1987-2000. *JAMA* 2004; 292: 2372- 2378.

- Brunekreef, 1994: Even after removing all observations with hourly ozone concentrations greater than 60 ppb, researchers found a decline in lung function and an increase in respiratory symptoms in this group of amateur cyclists.
- Brauer 1996: Even after excluding all days when the ozone was greater than 40 ppb, investigators still observed reduced lung function in a cohort of outdoor workers.
- Mortimer 2002: After excluding days when 8-hour average ozone was greater than 0.080 ppm, the associations with morning lung function decrements remained statistically significant.
- Bell, 2004: Estimates of premature mortality attributable to ozone changed little when days with 24-hour average concentrations greater than 0.06 ppm were excluded.
- Bell, 2006: There was little difference in the mortality effect estimate when days with 24-hour ozone concentrations above 0.02 ppm were excluded.

Focusing on Study Locations That Would Meet Various Standards Indicates the Standard Can be Set No Higher than 60 ppb

EPA's circumscribed examination of the epidemiological evidence focuses on North American studies that would have met various standards levels. Such an analysis provides a powerful argument that a standard of 75 is not protective of human health.

The further exploration of alternate standard levels in Table 4-1 from the *Policy Assessment* further demonstrates that even with a standard of 60 ppb, a number of study locations (where there were associations with adverse effects) would remain.

The *Policy Assessment* indicates that the reported effects estimates in these studies are largely influenced by locations meeting the potential alternative standards.

This analysis indicates that the standard can be set no higher than 60 ppb.

Table 4-1. Numbers of epidemiologic study locations likely to have met potential alternative standards with levels of 70, 65, and 60 ppb

			Number of study cities meeting potential alternative standards during entire study period		
Study	**Result**	**Cities**	**70 ppb**	**65 ppb**	**60 ppb**
Cakmak et al. (2006)	Positive and statistically significant association with respiratory hospital admissions	10 Canadian cities	7	6	2
Dales et al. (2006)	Positive and statistically significant association with respiratory hospital admissions	11 Canadian cities	5	4	0
Katsouyanni et al. (2009)	Positive and statistically significant associations with respiratory hospital admissions	12 Canadian cities	9	9	5
Katsouyanni et al. (2009)	Positive and statistically significant associations with total and cardiovascular mortality	12 Canadian cities	7	5	1
Mar and Koenig (2009)	Positive and statistically significant associations with asthma emergency department visits	Single city: Seattle	0	0	0
Stieb et al. (2009)	Positive and statistically significant association with respiratory emergency department visits	7 Canadian cities	5	4	3

<u>Cutpoint Analysis of Mortality Study Points to the Inadequacies of a Standard of 70 0r 65 ppb to Protect Public Health</u>

The draft *Policy Assessment* contains a "cut-point analysis" exploring the U.S. multicity study by Bell et al. (2006) reporting an association between short-term ozone concentrations and increased risk of premature death. The analysis presented in Table 4-2 focuses on the lowest cut-point for which the association between ozone and mortality was reported by be statistically significant, 30 ppb.

Table 4-2. Number of study cities with 3-year averages of 4th highest 8-hour daily max concentrations greater than 70, 65, or 60 ppb, for various cut-point analyses presented in Bell et al. (2006)

	Cut-point for 2-day moving average across monitors and cities (24-h avg)								
	25	30	35	40	45	50	55	60	All
Number (%) of Cities with 4th highest >70 (any 3-yr period; 1987-2000)	0 (0%)	16 (16%)	55 (56%)	82 (84%)	89 (91%)	92 (94%)	94 (96%)	95 (97%)	95 (97%)
Number (%) of Cities with 4th highest >65 (any 3-yr period; 1987-2000)	3 (3%)	35 (36%)	77 (79%)	89 (91%)	94 (96%)	95 (97%)	95 (97%)	95 (97%)	95 (97%)
Number (%) of Cities with 4th highest >60 (any 3-yr period; 1987-2000)	16 (16%)	61 (62%)	86 (88%)	94 (96%)	95 (97%)	96 (8%)	96 (8%)	96 (8%)	96 (8%)

According to the *Policy Assessment*, the analysis suggests that the majority of the air quality distributions that provided the basis for a positive and statistically significant association with mortality would have been allowed by a standard with a level of 70 or 65, while 40 percent of the cities would have met a standard of 60 ppb.

This rigorous analysis shows that cities that would have met a standard of 70 or 65 ppb were shown to have positive and significant associations with increased risk of premature death. This demonstrates that an upper end of the range at 70 or 65 ppb will fail to protect public health.

<u>New Evidence of Health Effects from Long-Term Exposures Must be Factored in to Standard Setting</u>

In this review, there is now considerable new evidence that chronic exposures to ozone can lead to adverse respiratory effects. In fact, the ISA now deems the strength of the evidence to be "likely causal," as compared to "suggestive" in the last review.

As we pointed out earlier, the ISA cites new evidence of increased risk of new onset asthma at mean annual 8-hour maximum concentrations of **55.2 ppb**, and increased risk of hospital admissions for children with asthma at mean annual 8-hour maximum ozone concentrations less than **41 ppb.** Furthermore, several new epidemiologic studies link ozone exposures of **69 ppb** (mean 8-hour maximum concentration) to inflammation and injury to the lung tissue.

The draft *Policy Assessment* makes the case that EPA will depend upon the 8-hour standard to protect against the effects of long-term concentrations. If that is the

case, these data points suggest that 70 ppb is not viable as the upper end of the range, and provide additional support for a standard of 60 ppb or below.

POLICY ASSESSMENT SHOULD INCLUDE DISCUSSION OF INTERNATIONAL STANDARDS

Representatives of the California EPA and the California Office of Health Hazard Assessment testified at the March 23-25, 2014 CASAC meeting that the California ozone air quality standard adopted in 2005 of 0.070 ppm "not to be exceeded" was equivalent to a 60 ppb standard with the federal form (Annual fourth-highest daily maximum 8-hr concentration, averaged over 3 years). Information on ozone air quality standards adopted by states, other countries, and recommended by the World Health Organization is pertinent to the review of the NAAQS and should be included in the *Policy Assessment*.

RISK AND EXPOSURE ASSESSMENT

EPA has undertaken a *Risk and Exposure Assessment* to characterize the potential public health implications of current and proposed alternative standards.

The draft *Risk and Exposure Assessment* clearly demonstrates the burden that current concentrations of ozone pose to public health, the inadequacy of the current standard of 75 ppb (8- hour average) to provide the legally required protection, and the reductions in exposure and risk that could be achieved with an alternative standard of 60 ppb.

Treatment of Background Concentrations is in REA is Appropriate

There is no evidence that the lungs respond differently to ozone from different sources. The Lung Association supports the assessment of risks from both natural and anthropogenic sources of ozone, as was done in the second draft REA.

There are several ways in which the REA should be improved.

Infants and Small Children Should be Included

First, children aged zero to five are one of the most susceptible populations, but they are not included in the quantitative risk and exposure assessment.

We know that the lungs are not fully developed at birth, and that ozone exposure can affect the post-natal development of the lungs. Infants are exposed to outdoor air and they are active outdoors from the time they are mobile. They experience higher exposures than adults because of their increased breathing rate. The REA should include infants and young children in the analysis.

Expand Consideration of Health Endpoints

Second, it should be emphasized that the health endpoints considered in the REA are limited, and do not represent the comprehensive array of health effects attributable to ozone exposure. For instance, the analysis mainly looks at lung function decrements, respiratory hospitalizations, and mortality. Respiratory emergency room visits are considered in only two cities, and respiratory symptoms in only one city.

Incorporating additional health endpoints, for a larger number of cities, would provide a clearer picture of the full spectrum of health effects of concern.

Evaluate Alternative Standards Down to 55 ppb

Third, the analysis only considers alternative levels of the standard of 70, 65, and 60 ppb, but our reading of the health literature indicates that a standard below 60 ppb, such as 55 ppb may be necessary to protect public health.

With chamber studies indicating adverse effects in healthy young adults at concentrations of 60 ppb, it is clear that more stringent standards, such as 55 ppb or below, must be considered to protect the health of children and people with lung disease.

Also, the risk assessment does not consider the public health implications of **alternative forms** of the standard. For instance, a "not to be exceeded" form, or alternative averaging times, or other possible forms should be evaluated.

We would like to see the final REA look at potential standards of 55 ppb, and to consider whether alternative forms of the standard can provide increased protection of public health.

The Emission Control Strategies Modeled Are Limited

Finally, it should be emphasized that the emissions control strategies modeled in the draft REA are limited. Localities will consider many additional factors such as updated emissions inventories and a variety of NOx and VOC control measures that were not analyzed in the risk assessment. It would be useful to see how the results are impacted by considering VOC reduction strategies as well as NOx controls.

With these changes, the REA would present a more complete picture of the nature of health risks and the impact of alternative standards.

Implications for Standard Setting

Despite these limitations, it is clear from the draft *Risk and Exposure Assessment* that a standard of 70 or 65 ppb will not be sufficient to prevent exposures of concern in vulnerable populations such as children and children with asthma.