December 2, 2019

Administrator Andrew Wheeler
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington D.C. 20460

Sent via Regulations.gov.

Re: Comments on Docket ID No. EPA-HQ-ORD-2018-0274

Dear Administrator Wheeler:

The American Lung Association appreciates the opportunity to provide comments on the Integrated Science Assessment (ISA) for Ozone and Related Photochemical Oxidants (External Review Draft)—EPA/600/R-19/093.

EPA's revised review process undermines the protection of public health

The Lung Association continues to express our objections to the changes to the process that EPA has adopted in this review. EPA's changes restrict the full discussion and review of the available scientific evidence, undermining the core purpose of this process: to set standards that "protect health with an adequate margin of safety." While the Lung Association has long supported and, indeed, taken legal action to ensure the completion of the reviews in a timely manner, the Lung Association opposes the current process because it undermines the ability of CASAC and EPA to arrive at appropriate and adequate decisions on these standards. The revised process means that the decisions you make as Administrator on these standards could not be based on a thorough review of the evidence.

The review process adopted in 2006 followed an open, deliberative discussion led by CASAC of the changes needed to improve the process. Based on the desire to provide an informed and robust assessment of the information, EPA established a protocol that included separate reviews of two separate drafts of the critical documents, including a separate Risk and Exposure Assessment (REA). That process ensured that EPA would have

Advocacy Office:
1331 Pennsylvania Avenue NW, Suite 1425 North
Washington, DC 20004-1710
Ph: 202-785-3355 F: 202-452-1805

Corporate Office:
55 West Wacker Drive, Suite 1150 | Chicago, IL 60601
Ph: 312-801-7630 F: 202-452-1805 info@Lung.org

reached conclusions on the scientific evidence about health and welfare impacts before beginning work on the policy implications.

EPA has set up an unprecedented, flawed process to truncate the review of the particulate matter and the ozone NAAQS. With these changes, critical information that forms the basis of the decisions is absent or unresolved.

Time is extraordinarily limited for this draft ISA review and evaluation. EPA chose to wait to initiate this review until only two years were left in the five-year review cycle allowed under the Clean Air Act, despite these reviews traditionally requiring more than five years. EPA has allocated no time for a second draft ISA, which we continue to request for a thorough review of multiple complex questions.

EPA further restricts the review by having this document arrive at the same time for review as both draft Policy Assessments (PA) for particulate matter and ozone. This overlap is particularly egregious. Until the ISA is final, no final, reliable determination of the air quality criteria exists; that is, there is no full conclusion on the evidence which "accurately reflect[s] the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from presence to such pollutant in the ambient air." 42 U.S.C 7408(a)(2).

Without first finalizing the ISA, EPA impairs the determination of the relevant policy decisions in accessing the Draft PA. EPA should not have released the Draft PA until the agency finalized the ISA. EPA's current process unacceptably handicaps the review.

Further, EPA failed to appoint an independent scientific panel for the ozone review, a step that cost the CASAC and EPA essential expertise in the complex avenues that the documents explore. Such panels had served multiple CASAC reviews for decades. EPA offered flawed arguments for ending the practice: that under the Clean Air Act, only CASAC can advise EPA, and that having no independent advisory panel would expedite the review. Both arguments are specious. The independent panels have always provided expert assistance only to CASAC, which CASAC then used to advise EPA. The panels have worked closely with CASAC to assist in an accurate and thorough scientific review following the adopted schedule.

Not until CASAC itself acknowledged its limitations and requested assistance in a letter to you did EPA take limited steps to provide additional assistance. [1] EPA appointed a new pool of advisors who lacked experience in the NAAQS review process and ozone, and then mangled the process again by limiting advisory actions to one single panelist's opinion, by letter, in response to written questions. This restricted process eliminated the traditional approach that provided a more complete and open discussion with multiple, experienced panelists who contributed independent perspectives and deliberated their consensus recommendations on topics throughout the reviews of each document.

The shining light in this damaged process is the diligence and thoroughness of the EPA staff in preparing this assessment. In general, there is much to support in their assessment. They have attempted to provide a full, extensive review, despite the all-too-abbreviated timeline.

The Lung Association strongly urges EPA to issue a second draft ISA, appoint an independent CASAC advisory panel and restore the process that the Agency had previously followed successfully for decades to complete this review to protect public health.

Identified Health Effects Increase

As the Clean Air Act envisioned, the expanding research into the health impact of ozone has identified many systems at risk and health effects previously underappreciated. Collecting and assessing these studies form an essential process to providing adequate protection under the law. The Lung Association agrees with many of the conclusions of health effects from ozone but urges EPA to review and reconsider some determinations. An adequate review requires that EPA prepare and take comments on a second draft ISA before issuing a final ISA.

Respiratory health effects

As the draft ISA concluded, growing evidence firmly establishes that short-term exposures to ozone cause serious harm to respiratory health. The Lung Association agrees with the assessment that short-term ozone exposure causes respiratory effects and the "likely causal" conclusion about long-term exposure. In addition, some additional international studies offer increased information about the long-term exposures.

The draft ISA reinforces and expands respiratory health effects from short-term exposures identified in previous reviews. Many newer studies reinforce the findings that short-term ozone exposure severely worsens asthma, especially in children, increasing the emergency department (ED) visits and hospital admissions.[2] Large multi-city studies provided additional evidence of risks to people with chronic obstructive pulmonary disease (COPD), [3] including a Canadian study examining Ontario cities with significantly lower ozone than many in the U.S.[4] Many more studies provided growing evidence that short-term ozone exposure increases the risk of ED visits for respiratory infections, including pneumonia,[5] providing expanded evidence not available for the 2015 ISA.

EPA builds a powerful case for the long-term impacts on respiratory health, especially regarding new onset of asthma. Evidence for effect shows up clearly in the Southern California Children's Health Studies that documented that effect in three cohorts of children who benefited with fewer children developing asthma as the ozone levels dropped over time.[6] In Quebec, a large study tracked an increase of new asthma cases among 19 percent of the children even where long-term ozone levels were at low concentrations.[7] These long-term studies provide important evidence that a long-term ozone standard should be considered.

Several large studies have found that short-term and long-term ozone exposures can affect lung function in children; none of these seem to be discussed in the ISA.[8] That may be because most are outside of the U.S. and Canada, which EPA set as the sole countries for studies on respiratory impacts that this draft ISA would include.

One notable remainder is the consistent evidence that ozone can harm even young, healthy adults. The clinical trials reported in the 2015 ISA found that young adults suffered measurable decreased lung function—a recognized harmful health effect—at levels as low as 60 ppb, below the current standard.[9]

Cardiovascular Harm

The Draft ISA steps back EPA's 2013 ISA conclusion from ozone is "likely causal" for cardiovascular effects to "suggestive of a causal relationship." The evidence, however, has grown to show that short-term exposure does increase the risk of harm, especially ischemic strokes and arrhythmias, particularly in people with cardiovascular disease.[10] Further, the details may require more examination of the subsets of the population or disease. Some found increased risk of stroke in specific subpopulations in the studies, such as people aged 75 to 84.[11] Most telling, a large meta-analysis of 34 studies found an elevated risk of ischemic stroke, but not hemorrhagic stroke, increased by 2.45 percent for every 10 ppb increase in ozone.[12] That later study was not included in the draft ISA.

Mortality

EPA has stepped back its conclusions on a critical finding from the 2013 ISA, shifting its finding that short-term exposure to ozone was "likely causal" of total mortality to "suggestive of causality." The Lung Association urges EPA to reconsider that conclusion and to restore the "likely causal" finding in a second draft ISA. The evidence also shows that long-term exposure is associated with increased risk of death.

EPA reports on the multiple new studies, including a massive study of Medicare participants that found premature deaths associated with levels of ozone down to and below 60 ppb, while controlling for PM2.5.[13] This study and many others[14] (although not all) show consistent evidence that ozone increases the risk of premature death from respiratory harm with no evidence of a threshold. EPA also finds strong documentation of the biological plausibility for the respiratory morbidity. EPA concludes that the "strong evidence" is "consistent within and across disciplines, and provides coherence and biological plausibility for the positive respiratory mortality associations reported across epidemiologic studies."[15] EPA acknowledges that these findings are consistent with the findings in the 2013 ISA.

EPA seems to have shifted its causality determination on the questions raised in new research on the cardiovascular impacts of ozone on mortality. EPA raises questions that need resolution about some inconsistent evidence about the biological pathways for cardiovascular mortality.

However, EPA should not base its causality determination solely on the uncertainties in the new evidence about cardiovascular impacts when stronger, consistent evidence exists that ozone causes respiratory mortality. We recommend EPA return its determination to "likely causal" for total mortality based on the consistency and strength of the evidence of increased risk of premature death from ozone exposure based on respiratory morbidity.

Further evidence is in a new study looking at the impacts of long-term exposure to ozone on the specific causes of mortality. This study used the massive cohort in the NIH-AARP Diet and Health Study and found significant associations with premature deaths from cardiovascular and respiratory diseases.[16] The study found the effects continued after adjusting for co-pollutants. This study adds to similar findings as another large study of long-term exposure using a well-established cohort: the American Cancer Society cohort studied by Turner et al, 2016 found increased risk of premature deaths from respiratory causes, included COPD and pneumonia and influenza.

New Health Outcomes Identified

Metabolic impacts. The Lung Association supports the inclusion of the new evidence linking both ozone to metabolic effects. The identification of the "likely causal" impact of ozone from both short and long-term exposures provides much needed information that greatly expands the populations at risk.[17] Positive associations from long-term exposure with increased harm, including premature death for diabetics, provides crucial information about new risks to their health that the estimated 30.3 million people with diabetes in the U.S. need to know. [18]

Populations at risk should expand

The Lung Association supports the findings that these groups face greater risk from ozone pollution: children, older adults, people with asthma, outdoor workers, people with certain genetic variants and individuals with reduced dietary intake of vitamins E and C. However, we also support adding people with chronic obstructive pulmonary disease (COPD), cardiovascular disease, and people with low socio-economic status (SES) or who live in areas with low SES to that list. While questions still remain on the risks those groups face, growing evidence points to the need to acknowledge that "adequate evidence" exists for them to be considered at risk.

- People with COPD. As mentioned earlier, EPA's analysis identified ozone linked to increased risk of ED visits for people with COPD in three large, multicity studies conducted in the U.S. and Canada,[19] including in one study that found the increased risk continued when assessing the impact of co-pollutants.[20] EPA also found consistent toxicological evidence to support the mechanistic basis of their increased risk. Such evidence would support EPA considering people with COPD to the list of those with adequate evidence to show they are at risk.
- Low SES. Another group that deserves greater acknowledgment of their increased risk are individuals of lower socio-economic status (SES) and those who live in low-income

> communities. In the 2013 ISA, EPA determined that evidence "suggests" that they were at increased risk from ozone. In this draft, EPA concludes that the evidence continues to show that they experience increased risk for ozone-related hospital admissions and emergency department visits, but that "no recent information has been found that would inform or change" that conclusion. However, new studies cited in other parts of the draft ISA add to the evidence that people in low SES communities face greater risk. At least one study of three large U.S. cities was not included: O'Lenick et al (2017) found evidence that children living in low SES communities in Atlanta, Dallas, and St. Louis faced increased risk of premature death during days with higher ozone.[21]

Millions remain at risk. The lengthy list means that, literally, millions of Americans face increased risk from ozone pollution and deserve more protection. The Lung Association estimates that 25.2 million Americans have asthma, including 6.2 million children.[22] The most recent estimates of people with COPD from 2007 to 2010 found that around 8.5 million had received that diagnosis.[23] However, this likely underestimates the population with COPD. A 2017 study reported more than 18 million people had evidence of impaired lung function that was consistent with COPD.[24]

Outdoor workers. EPA needs to acknowledge the vast number of Americans who are exposed to high ozone because they work outdoors. EPA wisely recognizes that they are at risk but does not include the numbers of them in the assessment of at-risk populations. According to the U.S. Bureau of Labor Statistics (BLS), in 2016, "47 percent of the jobs held by civilian workers required work outdoors at some point during the workday." [25] That would total nearly 71.2 million people of the 151.4 million-person workforce in 2016.[26] More than 90 percent of construction, extraction and protective service jobs require outdoor work, according to BLS. Many of these individuals likely have chronic diseases that may place them at higher risk, so they may face even greater risk of exacerbations of their diseases because of their daily work. Many others are healthy young adults like those who experienced adverse effects from ozone exposures at 60 ppb in clinical trials. EPA must not assume that all at risk populations will simply "stay indoors."

Climate Change, AKA "Climate Effects"

EPA recognizes and provides a detailed summary of the impacts of ozone on the climate; however, the Lung Association disagrees with the statement in the summary explaining the need for the change in the title of this section of the draft ISA. In the 2013 ISA, EPA titled this chapter "Climate Change," whereas in this draft ISA, EPA has shifted to the term "Climate Effects." The summary and, indeed, the strong assessment that follows recognize that the growing evidence that tropospheric ozone causes radiative forcing and likely causes serious changes to temperature, precipitation and other aspects of climate. However, despite that, EPA states that "the revised title for this causal statement provides a more accurate reflection of the available evidence."[27]

Ozone is considered the third most important greenhouse gas, behind carbon dioxide and methane.[28] New evidence from the Intergovernmental Panel on Climate Change (IPCC) Fifth

Assessment Report reinforces the impact that ozone has on warming the earth through increased radiative forcing.[29]

Despite the title of this section, EPA has provided a substantive summary of the impact of ozone on climate. That finding also applies, albeit indirectly, to human health as the impacts of climate change on human health are also well-documented by U.S. Global Research Program, in the Fourth National Climate Assessment.[30]

Summary

The Lung Association urges EPA to develop a second draft of the ISA to include the changes recommended and to allow an adequate assessment of the impacts of this widespread air pollutant on human health and the environment. An adequate assessment would require an appropriately qualified independent interdisciplinary review panel that could properly consider the scientific evidence and develop consensus advice for the CASAC in their review. An adequate assessment would also need to be final before EPA progresses farther with the review of the Policy Assessment. Unfortunately, the abbreviated, rammed-through process EPA currently proposes to follow cannot provide the appropriate process needed to meet the Clean Air Act requirements for the national ambient air quality standards—to protect public health.

Sincerely,

Albert Rizzo, MD, FACP,
Chief Medical Officer
American Lung Association

[1] Cox L.A. 2019. Clean Air Scientific Advisory Committee Letter to A. Wheeler, U.S. Environmental Protection Agency. CASAC Review of the EPA's Integrated Science Assessment for Particulate Matter (External Review Draft – October 2018). EPA-CASAC-19-002, April 11, 2019.

[2] Zu K, Liu X, Shi L, et al. Concentration-response of short-term ozone exposure and hospital admissions for asthma in Texas. *Environment International*. 2017;104:139-145. doi:10.1016/j.envint.2017.04.006; Goodman JE, Loftus CT, Liu X, Zu K. 2017. Impact of respiratory infections, outdoor pollen, and socioeconomic status on associations between air pollutants and pediatric asthma hospital admissions. *PLoS ONE* 12: e0180522. http://dx.doi.org/10.1371/journal.pone.0180522; Winquist A, Klein M, Tolbert P, Flanders WD, Hess J, Sarnat SE. 2012. Comparison of emergency department and hospital admissions data for air pollution time-series studies. Environ Health 11: 70. http://dx.doi.org/10.1186/1476-069X-11-70.; Malig BJ, Pearson DL, Chang YB, et al. A Time-Stratified Case-Crossover Study of Ambient Ozone Exposure and Emergency Department Visits for Specific Respiratory Diagnoses in California (2005-2008). *Environ Health Perspect*. 2016;124(6):745-753. doi:10.1289/ehp.1409495; Sacks JD, Rappold AG, Davis JA, Richardson DB, Waller AE, Luben TJ. Influence of urbanicity and county characteristics on the association between ozone and asthma emergency department visits in North Carolina. *Environ Health Perspect*. 2014;122(5):506-512. doi:10.1289/ehp.1306940; Sarnat JA, Sarnat SE, Flanders WD, et al. Spatiotemporally resolved air exchange rate as a modifier of acute air pollution-related morbidity in Atlanta. *J Expo Sci Environ Epidemiol*. 2013;23(6):606-615. doi:10.1038/jes.2013.32; BarryV, Klein M, Winquist A, Chang HH, Mulholland JA, Talbott EO, Rager JR, Tolbert PE, Sarnat SE. 2018. Characterization of the concentration-response curve for ambient ozone and acute respiratory morbidity in 5 US cities. *J Expo Sci Environ Epidemiol*. http://dx.doi.org/10.1038/s41370-018-0048-7; Shmool JLC, Kinnee E, Sheffield PE, Clougherty JE. Spatio-temporal ozone variation in a case-crossover analysis of childhood asthma hospital visits in New York City. *Environmental Research*. 2016;147:108-114. doi:10.1016/j.envres.2016.01.020; Sheffield PE, Zhou J, Shmool JLC, Clougherty JE. Ambient ozone exposure and children's acute asthma in New York City: a case-crossover analysis. *Environ Health*. 2015;14(1):25. doi:10.1186/s12940-015-0010-2.

[3] Malig et al, 2016; Barry et al, 2018

[4] Szyszkowicz M, Kousha T, Castner J, Dales R. 2018. Air pollution and emergency department visits for respiratory diseases: A multi-city case crossover study. *Environ Res* 163: 263-269. http://dx.doi.org/10.1016/j.envres.2018.01.043.

[5] Malig et al, 2016; Xiao Q, Liu Y, Mulholland JA, et al. Pediatric emergency department visits and ambient Air pollution in the U.S. State of Georgia: a case-crossover study. *Environ Health*. 2016;15(1):115. doi:10.1186/s12940-016-0196-y.; Barry et al, 2018; Szyszkowicz et al 2018; Darrow LA, Klein M, Flanders WD, Mulholland JA, Tolbert PE, Strickland MJ. 2014. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol* 180: 968-977. http://dx.doi.org/10.1093/aje/kwu234.; Winquist et al 2012

[6] Garcia E, Berhane KT, Islam T, McConnell R, Urman R, Chen Z, Gilliland FD. 2019. Association of changes in air quality with incident asthma in children in California, 1993-2014. *JAMA* 321: 1906-1915. http://dx.doi.org/10.1001/jama.2019.5357.

[7] Tétreault L-F, Doucet M, Gamache P, et al. Childhood Exposure to Ambient Air Pollutants and the Onset of Asthma: An Administrative Cohort Study in Québec. *Environ Health Perspect*. 2016;124(8):1276-1282. doi:10.1289/ehp.1509838

[8] Fernández-Plata R, Rojas-Martinez R, Martínez-Briseño D, García-Sancho C, Perez-Padilla R. Effect of Passive Smoking on the Growth of Pulmonary Function and Respiratory Symptoms in Schoolchildren. *Rev Invest Clin*. 2016;68(3):119-127; Hwang B-F, Chen Y-H, Lin Y-T, Wu X-T, Leo Lee Y. Relationship between exposure to fine particulates and ozone and reduced lung function in children. *Environmental Research*. 2015;137:382-390. doi:10.1016/j.envres.2015.01.009; Jung S-W, Lee K, Cho Y-S, et al. Association by Spatial Interpolation between Ozone Levels and Lung Function of Residents at an Industrial Complex in South Korea. *Int J Environ Res Public Health*. 2016;13(7):728. doi:10.3390/ijerph13070728; Tsui H-C, Chen C-H, Wu Y-H, Chiang H-C, Chen B-Y, Guo YL. Lifetime exposure to particulate air pollutants is negatively associated with lung function in non-asthmatic children. *Environ Pollut*. 2018;236:953-961. doi:10.1016/j.envpol.2017.10.092; Urman R, McConnell R, Islam T, et al. Associations of children's lung function with ambient air pollution: joint effects of regional and near-roadway pollutants. *Thorax*. 2014;69(6):540-547. doi:10.1136/thoraxjnl-2012-203159; Karakatsani A, Samoli E, Rodopoulou S, et al. Weekly

Personal Ozone Exposure and Respiratory Health in a Panel of Greek Schoolchildren. *Environ Health Perspect*. 2017;125(7):077016. doi:10.1289/EHP635.

[9] U.S. EPA. Integrated Science Assessment (ISA) of Ozone and Related Photochemical Oxidants (Final Report, Feb 2013). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-10/076F, 2013..

[10] Carlsen HK, Forsberg B, Meister K, Gíslason T, Oudin A. Ozone is associated with cardiopulmonary and stroke emergency hospital visits in Reykjavík, Iceland 2003-2009. *Environ Health*. 2013;12(1):28. doi:10.1186/1476-069X-12-28; Guo P, Wang Y, Feng W, et al. Ambient Air Pollution and Risk for Ischemic Stroke: A Short-Term Exposure Assessment in South China. *Int J Environ Res Public Health*. 2017;14(9):1091. doi:10.3390/ijerph14091091; Liu H, Tian Y, Xu Y, et al. Association between ambient air pollution and hospitalization for ischemic and hemorrhagic stroke in China: A multicity case-crossover study. *Environ Pollut*. 2017;230:234-241. doi:10.1016/j.envpol.2017.06.057; Xu X, Sun Y, Ha S, Talbott EO, Lissaker CTK. Association between ozone exposure and onset of stroke in Allegheny County, Pennsylvania, USA, 1994-2000. *Neuroepidemiology*. 2013;41(1):2-6. doi:10.1159/000345138.

[11] Chen L, Villeneuve PJ, Rowe BH, Liu L, Stieb DM. The Air Quality Health Index as a predictor of emergency department visits for ischemic stroke in Edmonton, Canada. *J Expo Sci Environ Epidemiol*. 2014;24(4):358-364. doi:10.1038/jes.2013.82.

[12] Yang W-S, Wang X, Deng Q, Fan W-Y, Wang W-Y. An evidence-based appraisal of global association between air pollution and risk of stroke. *Int J Cardiol*. 2014;175(2):307-313. doi:10.1016/j.ijcard.2014.05.044.

[13] Di Q. Wang Y, Zanobetti A, Wang Y, Koutrakis P, Choirat C, Dominici F and Schwartz JD. 2017. Air pollution mortality in the Medicare population. *NEJM*. 376(26): 2513-2522.

[14] Madrigano J, Jack D, Anderson GB, Bell ML, Kinney PL. Temperature, ozone, and mortality in urban and non-urban counties in the northeastern United States. *Environ Health*. 2015;14(1):3. doi:10.1186/1476-069X-14-3; Liu T, Zeng W, Lin H, et al. Tempo-Spatial Variations of Ambient Ozone-Mortality Associations in the USA: Results from the NMMAPS Data. *Int J Environ Res Public Health*. 2016;13(9):851. doi:10.3390/ijerph13090851; Jhun I, Fann N, Zanobetti A, Hubbell B. Effect modification of ozone-related mortality risks by temperature in 97 US cities. *Environment International*. 2014;73:128-134. doi:10.1016/j.envint.2014.07.009; Moolgavkar SH, McClellan RO, Dewanji A, Turim J, Luebeck EG, Edwards M. Time-series analyses of air pollution and mortality in the United States: a subsampling approach. *Environ Health Perspect*. 2013;121(1):73-78. doi:10.1289/ehp.1104507; Peng RD, Samoli E, Pham L, Dominici F, et al. 2013 Acute effects of ambient ozone on mortality in Europe and North America: results from the APHENA study. *Air Quality, Atmosphere & Health*. 6(2) 45-452. doi.org/10.1007/s11869-012-0180-9. ; Bravo MA, Son J, de Freitas CU, Gouveia N, Bell ML. Air pollution and mortality in São Paulo, Brazil: Effects of multiple pollutants and analysis of susceptible populations. *J Expo Sci Environ Epidemiol*. 2016;26(2):150-161. doi:10.1038/jes.2014.90; Requia WJ, Adams MD, Arain A, Papatheodorou S, Koutrakis P, Mahmoud M. Global Association of Air Pollution and Cardiorespiratory Diseases: A Systematic Review, Meta-Analysis, and Investigation of Modifier Variables. *Am J Public Health*. October 2017:e1-e8. doi:10.2105/AJPH.2017.303839; Hao Y, Balluz L, Strosnider H, Wen XJ, Li C, Qualters JR. Ozone, Fine Particulate Matter, and Chronic Lower Respiratory Disease Mortality in the United States. *Am J Respir Crit Care Med*. 2015;192(3):337-341. doi:10.1164/rccm.201410-1852OC; Kravchenko J, Akushevich I, Abernethy AP, Holman S, Ross WG, Lyerly HK. Long-term dynamics of death rates of emphysema, asthma, and pneumonia and improving air quality. *Int J Chron Obstruct Pulmon Dis*. 2014;9:613-627. doi:10.2147/COPD.S59995; Turner MC, Krewski D, Diver WR, et al. Ambient Air Pollution and Cancer Mortality in the Cancer Prevention Study II. *Environ Health Perspect*. 2017;125(8):087013. doi:10.1289/EHP1249; Vanos JK, Hebbern C, Cakmak S. Risk assessment for cardiovascular and respiratory mortality due to air pollution and synoptic meteorology in 10 Canadian cities. *Environ Pollut*. 2014;185:322-332. doi:10.1016/j.envpol.2013.11.007

[15] EPA, Draft ISA p. 6-22.

[16] Lin CG, Hayes RB, Ahn J, Shao Y, Silverman D, Jones RR, Garcoa C, Bell ML, Thurston GD. 2019. Long-Term Exposure to Ozone and Cause- Specific Mortality Risk in the United States. *Am J Resp CC Med*. 2019. 200(8):1022; Turner et al., 2016.

[17] U.S. Environmental Protection Agency. Review Draft, Integrated Science Assessment for Ozone and Related Photochemical Oxidants (ISA). 2018, p. IS-8.

[18] Centers for Disease Control and Prevention. *National Diabetes Statistics Report*, 2017. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2017.

[19] Malig et al, 2016; Szyszkowicz et al 2018; Stieb, DM; Szyszkowicz, M; Rowe, BH; Leech, JA. (2009). Air pollution and emergency department visits for cardiac and respiratory conditions: A multi-city time-series analysis. Environ Health 8: 25. http://dx.doi.org/10.1186/1476-069X-8-25.

[20] Malig et al, 2016

[21] O'Lenick CR, Chang HH, Kramer MR, Winquist A, Mulholland JA, Friberg MD, Sarnat SE. 2017. Ozone and childhood respiratory disease in three US cities: evaluation of effect measure modification by neighborhood socioeconomic status using a Bayesian hierarchical approach. Environ Health. 16:36. Doi: 10.1186/s12940-017-0244-2

[22] Centers for Disease Control and Prevention. National Health Interview Survey, 2017. Analysis by the American Lung Association Epidemiology and Statistics Unit Using SPSS Software.

[23] CDC NHIS and American Lung Association analysis.

[24] Tilert T, Dillion C, Paulose-Ram R, et al. Estimating the U.S. Prevalence of Chronic Obstructive Pulmonary Disease Using Pre- and Post-Bronchodilator Spirometry: The National Health and Nutrition Examination Survey (NHANES) 2007-2010. Respiratory Research. 2013: 14(1):103.

[25] U.S. Department of Labor Bureau of Labor Statistics (BLS). "Over 90 percent of protective service and construction and extraction jobs require work outdoors. January 06, 2017. TED: The Economics Daily. Accessed 11/19/19 at https://www.bls.gov/opub/ted/2017/over-90-percent-of-protective-service-and-construction-and-extraction-jobs-require-work-outdoors.htm.

[26] BLS, Labor Force Statistics from the Current Population Survey. Household Data Annual Averages. 1. Employment status of the civilian noninstitutional population, 1948 to date. Accessed on 11/19/2019 at https://www.bls.gov/cps/cpsaat01.htm.

[27] EPA Draft ISA, p. 9-1.

[28] Forster P, Ramaswamy V, Artaxo P, Berntsen T, et al. 2007. Changes in atmospheric constituents and in radiative forcing. In: Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change [Solomon, S., D. Qin, M. Manning, Z. Chen, M. Marquis, K.B. Averyt, M. Tignor and H.L. Miller (eds.)]. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA.

[29] IPCC (Intergovernmental Panel on Climate Change). (2013). Climate change 2013: The physical science basis. Contribution of working group I to the fifth assessment report of the Intergovernmental Panel on Climate Change. In TF Stocker; D Qin; GK Plattner; MMB Tignor; SK Allen; J Boschung; A Nauels; Y Xia; V Bex; PM Midgley (Eds.). Cambridge, UK: Cambridge University Press. http://www.ipcc.ch/report/ar5/wg1/.,

[30] USGCRP, 2018. *Impacts, Risks, and Adaptation in the United States: Fourth National Climate Assessment, Volume II* U.S. Global Climate Change Research Program, Washington, D.C. USA. doi:10.7930/NCA4.2018.