# TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

*Protecting Texas by Reducing and Preventing Pollution*

March 24, 2014

Air and Radiation Docket and Information Center
Mail Code: 2822T
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW.
Washington, DC 20460

Attn: Docket ID No. EPA–HQ–OAR–2008–0699

Re: Comments on the U.S. EPA Second External Review Draft Policy Assessment for Ozone and Related Photochemical Oxidants EPA–452/P–14–002

Dear Sir or Madam:

The Texas Commission on Environmental Quality (TCEQ) appreciates the opportunity to respond to the U.S. Environmental Protection Agency's (EPA) request for input in the notice published in the January 29, 2014, edition of the *Federal Register* entitled: "Second External Review Draft Policy Assessment for Ozone and Related Photochemical Oxidants."

Enclosed, please find TCEQ's detailed comments to the EPA action referenced above. If you have any questions concerning the enclosed comments, please contact Michael Honeycutt, Ph.D., Toxicology Division, Office of the Executive Director, at michael.honeycutt@tceq.texas.gov.

Sincerely,

Richard A. Hyde, P.E.
Executive Director

Enclosure

# Policy Assessment Second Draft - 2014

In February of 2014, EPA released its second draft Policy Assessment for Ozone for public comment closing on March 24th 2014. At the same time, the second draft Welfare Risk and Exposure Assessment and second draft Health Risk and Exposure Assessment (HREA) were released for public comment with the same closing date, allowing stakeholders 36 working days to review the three substantial documents and all associated appendices. This is impracticable and suggests that EPA is not interested in receiving meaningful and complete comments. If EPA genuinely wishes to receive the most useful input, advanced notice should be given to stakeholders paired with a reasonable timeframe for preparing comments. Nevertheless, in the time allowed, TCEQ has prepared the following comments on the second draft Policy Assessment.

The draft Policy Assessment (PA) states that it draws upon the HREA, but it is unclear how it could do so. If the HREA and PA are released at the same time, it is impossible for EPA to consider public comments and CASAC advice on the HREA in the PA.

EPA has not made the case that a lower standard will improve public health and TCEQ urges EPA to retain the current standard.

## General Comments

The TCEQ agrees with EPA that the NAAQS for ozone should protect public health. We would like to emphasize that modeling presented in the HREA indicates a lower standard may result in additional premature mortality for some areas of the country, including Houston (figures 7B-2 and 7B-4). By EPA's own calculations, lowering the standard from the present condition to 70, 65, or 60 ppb is predicted to result in 41, 35, or 22 increased deaths in Houston. Clearly, lowering the ozone standard is not predicted to result in public health benefits for Houstonians.

TCEQ would like to emphasize the following text taken from the PA:

> "On July 23, 2013, the D.C. Circuit Court of Appeals upheld EPA's 2008 primary $O_3$ standard, but remanded the 2008 secondary standard to the EPA. State of Mississippi v. EPA. 723 F. 3d 246...The court went on to reject arguments that EPA should have adopted a more stringent primary standard... With respect to the epidemiologic evidence, the court accepted EPA's argument that there could be legitimate uncertainty that a causal relationship between $O_3$ and 8-hour exposures less than 0.075 ppm exists, so that associations at lower levels reported in epidemiologic studies did not necessitate a more stringent standard."

Because there have been no substantial changes in state of the available science between July 2013 and February 2014, and the weight of evidence continues to indicate that the current standard is adequately protective, it is unclear why EPA is contemplating such a drastic change in the ozone standard. The TCEQ agrees with EPA's arguments in the

D.C. Circuit Court of Appeals that "...associations at lower levels reported in epidemiologic studies did not (and do not) necessitate a more stringent standard."

In addition, the lower end of the proposed range of alternative $O_3$ standards is not well-supported. In fact, EPA states that at lower concentrations "...the likelihood and magnitude of a response becomes increasingly uncertain..." (p3-1) and elsewhere that the "...the relative importance of background $O_3$ would increase ...with a lower level of the $O_3$ NAAQS" (p2-27).

The Executive Summary of the PA gives only cursory mention of important issues such as uncertainty in causal determinations, existence of thresholds, regional heterogeneity and non-adverse nature of key endpoints. The result is that this section gives a wholly inaccurate and incomplete description of the evidence that does or does not support a lower NAAQS.

**A true Weight of Evidence is lacking.**

EPA has not applied a rigorous weight of evidence framework to integrate results from human clinical studies, epidemiological studies, and animal studies. Throughout the document, studies are described as "positive" without indicating whether the results were statistically significant, biologically plausible or clinically meaningful, or consistent with other studies. For example, newer studies (Smith *et al.* 2009, Zanobetti and Schwartz 2008, and Jerrett *et al.* 2009) were not weighed against other studies that reported "small associations or no associations" between ozone and mortality (p3-36). This practice results in an inaccurate perception that most of the available evidence supports a causal relationship between levels of ozone below the current standard and purported health effects.

In its consideration of weight of evidence, it is not clear how EPA evaluated consistency across studies or whether evidence evaluated across realms was ultimately considered. For example, how likely are the associations between cardiovascular mortality when cardiovascular morbidity endpoints are inconsistent and not generally supportive of the mortality endpoints? In addition, it is not clear how the evidence laid out in the PA leads EPA to determine there is likely to be a causal relationship between short-term exposure to $O_3$ and cardiovascular system effects, including mortality, because EPA has described this evidence as "inconsistent" and "confounded by other pollutants."

A rigorous weight of evidence evaluation should be conducted, rather than giving positive results more weight than null results simply because they are positive. Based on EPA's incomplete evaluation of the evidence, it is not clear that there are causal relationships for health effects at ozone exposures below the current standard. The TCEQ urges EPA to use a rigorous weight of evidence as recommended by the National Academy of Sciences (NAS), and believes that EPA should not make policy judgments without assessing all of the available evidence.

**The selection of endpoints is inappropriate in some cases.**

The PA uses endpoints previously determined to have "Suggestive," "Likely Causal" as well as "Causal" relationships with ozone exposure. TCEQ believes only endpoints with

sufficient evidence to indicate a causal association should be used in setting a NAAQS. We agree that at high levels of exposure, respiratory effects can occur. Therefore, only respiratory endpoints that can be demonstrated to be caused by short-term exposure to ozone should be used. It is especially problematic to use mortality supposedly related to long-term exposure to ozone as this was categorized as merely "Suggestive" in ISA and lacks adequate evidence from scientific literature to be utilized in setting a standard.

In the 2013 ISA, EPA stated that the epidemiology evidence for cardiovascular endpoints is inconsistent and lacks coherence across realms of evidence. In addition, Goodman *et al.* (2014) rigorously evaluated the studies reviewed by EPA as well as additional available literature. The authors utilized a systematic weight of evidence approach and determined that the available studies reported mixed results with positive, null and negative associations being reported. These results indicate that there is not adequate evidence of a causal relationship and therefore cardiovascular endpoints should not be included in the PA.

Throughout the PA, EPA continues to reiterate its belief that ozone causes asthma. In fact, CASAC has repeatedly emphasized the limited evidence for new-onset asthma. In addition, it is not clear that the findings of two multi-city studies, Schildcrout *et al.* (2006) and O'Connor *et al.* (2008) have been considered. In fact, it is more accurate to say that there is significant uncertainty surrounding the evidence for this endpoint and references to this endpoint should be removed from the document.

In addition, one of the key endpoints used by EPA to justify a lower standard is single occurrences of small decrements in lung function in the absence of respiratory effects. The clinical studies utilized in EPA's analysis indicate decrements in $FEV_1$ much smaller than 10% would be expected from exposure to levels of ozone proposed as alternative standards. In fact, EPA states on page 3-57 "...some experts would judge single occurrences of moderate responses to be a 'nuisance.'" This is an accurate description as these lung function decrements would be transient, reversible, would not interfere with normal activity and would not result in permanent injury or respiratory dysfunction (Goodman *et al.* 2013).

Finally, EPA does not provide confidence bounds that reflect the uncertainty in these estimates and therefore fails to explain whether a lower standard would result in statistically significant changes in these endpoints. We would also like to emphasize that the standard is based on the 4$^{th}$ highest 8-hour concentration averaged over 3 years. Based on this, it is unclear how estimates of one or two days over 60 ppb or one or two occurrences of 10% $FEV_1$ decrements supports a lower standard that would not necessarily prevent a single occurrence as apparently suggested by EPA.

The TCEQ urges EPA to only use causal endpoints and to select endpoints that have clear biological plausibility and clinical significance. Moreover, the available data indicate that adverse respiratory effects do not occur at ozone concentrations below the current NAAQS.

**The classification of "at risk" groups is not adequately supported.**

The PA indicates that EPA classifies children and asthmatics as "at risk" groups in its analysis. EPA extrapolated lung function data from 18 to 35 year old volunteers to

younger age groups and support this decision by saying that change in lung function in children is similar to adults. EPA appears to be contradicting itself, and it is therefore unclear how this observation supports classifying children as an "at risk" group. In addition, on page 3-99 of the PA we would like to emphasize that EPA states "the percentage of asthmatic children estimated to experience such decrements is virtually the same as the percentage estimated for all children." Later, EPA states that children without asthma are estimated to experience lung function decrements that are "virtually indistinguishable" from non-asthmatics (p4-27). Moreover, on page 30-105, the PA indicates that evidence for differences between asthmatics and non-asthmatics has been mixed. The TCEQ agrees with the observation that asthmatics are not at increased risk and urges EPA to clearly communicate this throughout the document, especially in the Executive Summary.

**There is evidence for effect thresholds that is not utilized in the PA.**

EPA indicates that it does not believe there to be a population threshold for effects of ozone based on its review of relevant epidemiology. However, there are a number of factors that limit the ability to detect thresholds in such studies. It has long been recognized that measurement error can bias results, which tends to flatten and linearize exposure-response curves in epidemiological studies (Rhomberg *et al.* 2011). Brauer *et al.* (2002) have also evaluated exposure misclassification for ozone where ambient concentrations are very poor approximations of personal exposure. The authors find that it is not possible to determine whether or not an effect threshold exists. Therefore, the conclusion that there is no evidence to support a threshold for ozone exposure and mortality is not supported, and the evidence from controlled human exposure studies as well as proposed modes of action should be used to support the existence of a threshold for purported mortality effects.

Chapter 3 of the PA contains an inaccurate description of the threshold used in the MSS model (p3-98), which the HREA clearly states to be not a concentration threshold. In fact, the McDonnell (2012) study does indicate the existence of a concentration threshold that should be included in EPA analysis. The authors defined a threshold of 59 ppb and concluded that the threshold model fit the data better than a non-threshold model. Moreover, the studies by Adams (2002 and 2006), Schelegle *et al.* (2009), and Kim *et al.* (2011) all indicate a threshold below 70 ppb at which there are not statistically significant adverse effects associated with ozone.

CASAC provided EPA with advise that is in agreement with the above comments: "...the recent paper by McDonnell *et al.* 2012 clearly establishes the statistical significance of a threshold model for $O_3$ $FEV_1$ responses...the model would also be directly applicable to functional changes seen in...epidemiology studies." The commenter continued "[j]ust because the epidemiology studies are not able to define a threshold for $O_3$ effects for the mortality, hospital admissions, and other effects does not mean that a 'biologically effective threshold' does not exist. This issue becomes a statistical one that epidemiology studies have a difficult time trying to establish. However, most biomedical scientists would argue that there is a threshold." The TCEQ agrees with this member of CASAC and encourages EPA to appropriately incorporate thresholds into their analysis.

**Risk is calculated below background and lowest measured levels of relevant studies.**

In the PA, EPA acknowledges that there is uncertainty in extrapolating health risks from ozone exposures that go beyond the ozone levels measured in the relevant epidemiology. However, EPA presents analysis on "total" risk modeled down to zero, outside of the range of available data. This is problematic because there is no way to determine the uncertainty surrounding the risk estimates for the alternative standards under consideration.

In reviewing the studies cited by EPA in the PA, associations between ozone and selected endpoints generally became weaker and not significant at lower ozone levels. EPA did not incorporate these findings in its risk assessment. Instead, risks were extrapolated below the LMLs of the selected studies and to zero ozone, even though the data from the underlying studies did not report effects at low levels of ozone.

Perhaps more importantly, in assigning risk below background levels of ozone, EPA is suggesting risk below levels that can be potentially modified by implementation of the ozone NAAQS, as emphasized by CASAC in its review of the first draft HREA. In fact, one member of CASAC stated "The C-R function which goes down to zero makes little sense. First of all, such levels are never obtained... Secondly, this zone has little value since it cannot be influenced by the regulatory process." This commenter continues "...we should have a vision of what levels/cut offs are scientifically sound and contribute to standard setting in a practical way." A second commenter added "[g]iven the background levels of $O_3$ that cannot be controlled by U.S. regulatory actions, this reviewer endorses applying the C-R function down to the LML and does not support obtaining risk estimated down to zero."

Given the uncertainty surrounding risks calculated at low levels of ozone, the TCEQ urges EPA to assess risk above background ozone levels, as these are the levels that can potentially be controlled by regulation.

**Background should be considered when setting the ozone NAAQS.**

EPA estimates background ozone constitutes as much as 80% of the total seasonal mean $O_3$ in areas of Texas. This calls into question the reasonableness of the proposed alternative standards. EPA states "[p]roximity to background levels could be an additional consideration..." when setting the NAAQS (p2-27). The TCEQ urges EPA to appropriately consider background when setting the NAAQS for ozone.

**Clinical studies provide useful information in the context of standard setting.**

TCEQ agrees that human clinical studies provide important policy-relevant information. This includes the following observations:

- Effects approaching biological and statistical significance are not reliably observed at concentrations <80 ppb.

- Effects observed at lower concentrations are generally mild, transient, and of questionable biological and statistical significance.
- Based on information provided in the REA, exposures estimated to result in decrements in lung function >10% occur infrequently under conditions where the current standard is met and as stated by EPA "...some experts would judge single occurrences of moderate responses to be a 'nuisance,'" (p3-57).

In the PA, EPA describes the exercise patterns in the clinical studies examining lung function as "moderate" when individuals exercised 50 minutes of each hour for a prolonged period of 6.6 hours. However, as noted in Folinsbee *et al.* 1988 and McDonnell *et al.* 1991, this simulates work performed during a day of heavy manual labor in outdoor workers. In fact, exercise at this level for 6 to 8 hours should be considered as "heavy" or "strenuous" instead. We would like to emphasize that CASAC commented on this in the first draft HREA, saying the clinical studies cited by EPA used "...unrealistic elevated minute ventilations" and that "overall ventilations are ≥ mean ventilations that might be encountered during a day of heavy severe manual labor and represents the higher end of ventilations that might be encountered in the normal population for this prolonged period (6.6 h)."

It is troubling that the PA repeatedly misrepresents the results of the Adams 2006 study and the treatment of this data by EPA (i.e., Brown *et al.* 2007 and 2008). For the sake of transparency, it should be clear throughout the document that Adams 2006 did not report statistically significant effects at 60 ppb ozone. However, EPA chose to reanalyze a portion of the data from this study using different statistical methods and generated small, but statistically significant results. The original study author disagreed with the procedure followed by EPA in reanalyzing his data. The TCEQ agrees that EPA's reanalysis of Adam's data using t-tests rather than a multiple comparison test is inappropriate. As such, all tables in text throughout the text should correctly cite the non-significant findings and, if necessary, include a footnote explaining EPA's re-analysis and the fact that its approach is disputed.

EPA states on page 3-11 that "mean $FEV_1$ is clearly decreased by 6.6-h exposure to 60 ppb $O_3$." However, this is a misrepresentation of the available data. For example, in Table 3-1 EPA presents data that does not support this statement. Moreover, when coupled with the information presented in the previous comment, it is clear that exposure to ozone below 60 ppb does not result in mean $FEV_1$ decrements. This erroneous language should be removed.

EPA cites critical guidance issued by the American Thoracic Society (ATS) in 2000 on page 3-14, footnote 14. Namely that reversible loss of lung function is not adverse in the absence of respiratory symptoms. Such an important point should not be relegated to a footnote. In addition, the description of the ATS 2000 recommendations is inconsistent throughout the document. The document should describe $FEV_1$ decrements in this context uniformly throughout the text. In addition, the most recent ATS guidance should be cited throughout the PA.

Finally, TCEQ has concerns regarding the results of the MSS modeling presentenced in the HREA as they apply to the PA. We would like to emphasize that the studies utilized in this model do not demonstrate $FEV_1$ decrements greater than 10% following exposure

to 60 ppb ozone. Moreover, the results presented for the MSS model indicate that a ~7% FEV1 decrement might be predicted for individuals exposed to 100 ppb ozone while exercising strenuously for 6.6 hours. It is clearly not biologically feasible that this model predicts much greater decrements (>10%, 15% and 20%) for much lower ozone concentrations of 60, 70 and 80 ppb. Therefore, the PA is poised to make policy recommendations based on suspect modeling results and an incomplete and inaccurate presentation of the scientific literature.

TCEQ urges EPA to utilize only adverse effects in its analysis, rather than questionable metrics such as ≥10% $FEV_1$ decrements that may occur only once per year. EPA has not made the case that this mild, transient, reversible effect is adverse nor has it established that adverse effects occur at ozone concentrations below the current standard.

**Epidemiology studies are limited by their study design.**

In its discussion of the available epidemiological studies, there is inadequate discussion of personal exposure and indoor versus outdoor ozone concentrations. EPA should consider such differences when interpreting studies reporting associations between health effects and ambient ozone concentrations. How likely are these associations to be plausible given estimates of personal exposure? The TCEQ believes it is highly unlikely that these associations are plausible.

In addition, EPA introduces the topic of regional heterogeneity and states that "a national or combined analysis may not be appropriate..." in the context of discussion thresholds. However, this also calls into question the appropriateness of a one-size-fits-all standard. The observed city to city heterogeneity strongly implies such as standard would be more or less stringent than necessary, depending on location.

In a number of places, EPA appears to be mischaracterizing the findings from key studies. For instance, the text seems to be missing the main point of the data presented in figure 3-4; namely that there is no increased risk below ~50 ppb (based on the point at which the CI doesn't appear to include 1.0). Similarly, in the discussion of figure 3-6 the data indicate no significant risk until ozone concentrations exceed 70 ppb. This is missing from the discussion of this data. It is also unclear how this data supports the lower end of the proposed range

In conclusion, the available epidemiology studies have reported substantial heterogeneity between cites that range from positive to null or negative (i.e. higher ozone levels are correlated with reduced mortality). Therefore, a pooled nation-wide estimate is misleading. Moreover, the TCEQ believes that ecological epidemiology studies are not rigorous enough to use as the basis for setting the ozone standard and urges EPA to use a quantitative weight-of-evidence approach that includes all available information.

**Ambient concentrations are not representative of personal exposures.**

EPA should explain the limitations of setting standard for ambient air based on clinical exposures when HREA states that most people spend the majority of their time indoors. Presumably, the patients in the epidemiology studies used by EPA to propose lowering

the standard also spent much of their time indoors. Similarly, it is unclear how the results of APEX modeling in the HREA were paired with the information from the DEARS (Meng *et al.* 2012), Xue *et al.* 2004 and Geyh *et al.* 2000 studies which indicate that daily personal exposure is well below any of the benchmarks suggested. In addition, the U.S. Energy Information Administration estimates that for many areas of the country, as much as 98.4% of the population utilizes air conditioning units, which remove the vast majority of ambient ozone.[1]

EPA considers outdoor workers to be an "at risk" population that may be exposed to levels of ozone reported at ambient monitors. A study by O'Neill *et al.* 2003 reported that outdoor workers in Mexico City experienced average personal ozone exposures that were 60 percent lower than ambient monitor levels. EPA also suggests that children playing outside for extended periods of time may be exposed to levels of ozone reported at ambient monitors. In a study by Lee *et al.* 2004, children in the top 25% of time spent outdoors experienced personal ozone exposures 80% lower than levels measured at ambient monitors. This difference between ambient ozone concentrations and personal exposures is key for interpreting both epidemiological studies as well as clinical exposure studies. In fact, EPA is aware that there are differences between ambient concentrations of ozone and personal exposure, but effectively ignores this difference in the HREA when deriving quantitative estimates of risk.

EPA points out in figure 5-15 that the upper end of daily average ozone personal exposure are well less than 20 ppb, well below the current standard and the range of proposed alternate standards. The TCEQ urges EPA to consider personal exposure in setting the ozone standard, which would lead to the conclusion that the current standard is more than adequately health–protective.

**There is substantial evidence for confounding by co-pollutants.**

The PA indicates that the analysis presented is "relatively robust" to inclusion of PM. However, EPA noted in the first draft HREA that confounding by co-pollutants reduces the effect estimates for ozone. Therefore EPA should acknowledge that risk estimates may well be overestimated by not using multi-pollutant models. In fact, CASAC also commented on this point: "[t]o this reviewer, no results should be presented that have not taken into account $PM_{2.5}$ at a minimum." This topic is especially troubling as the additional analysis presented in Appendix 7 of the HREA demonstrates that upon inclusion of $PM_{10}$ in a co-pollutant model; virtually all of the risk estimates for short-term mortality related to ozone exposure become non-significant.

The TCEQ urges EPA to utilize multipollutant models that account for the confounding effects of co-pollutants and better capture the potential contribution of ozone to health effects.

**Mortality analysis in the HREA is especially problematic.**

[1] http://www.eia.gov/consumption/residential/reports/2009/air-conditioning.cfm

Important information presented in the HREA is not adequately communicated in the main text of the PA. EPA estimates short-term mortality impacts based on Zanobetti and Schwartz (2008) and Smith *et al.* (2009). However, the Concentration Response Functions (CRFs) vary from negative to positive for the same city, depending on which study is selected, ozone averaging time, model specifications, and ozone season. In fact, many of these estimates are indistinguishable from zero. It is not clear how these issues were considered by EPA or how the various choices of CRFs were weighed. In addition, these studies also indicate the confounding effects of co-pollutants such as PM and sulfate, which were not adequately considered by EPA as single pollutant CRFs were utilized in the core analysis.

EPA also estimates long term mortality impacts based on Jerrett *et al.* 2009. However, on page 3-41 EPA indicates that there is "limited evidence for an association between long-term exposure to ambient $O_3$ concentrations and respiratory mortality." We would like to emphasize that long-term mortality was not listed in the HREA as an ozone-attributable effect nor is it listed as a causal endpoint in ISA. The use of this study is concerning, as other studies of this cohort reported no associations between long-term ozone exposure and cardiopulmonary mortality that are robust to adjustment for co-pollutants (e.g., Krewski *et al.* 2000; Pope *et al.* 2002). In addition, other long-term studies of ozone-related respiratory or cardiopulmonary mortality did not report positive associations (Dockery *et al.* 1993; Beeson *et al.* 1998; Abbey *et al.* 1999; Chen *et al.* 2005; Miller *et al.* 2007; Lipfert *et al.* 2000 for mean $O_3$; Lipfert *et al.* 2006; Wang *et al.* 2009; Jerrett *et al.* 2005). Moreover, it is inappropriate to combine data across cities for a national risk estimate, given the known geographic heterogeneity of these estimates (Smith *et al.* 2009)). In addition, data relating to potential confounders was collected in 1982–1983 for the ACS study but never updated. For these reasons, the national risk estimate reported by Jerrett *et al.* (2009) should not be extrapolated throughout the U.S.

In the HREA, Figure 7-2 presents heat maps for short-term ozone-attributable mortality. It is unclear how 149 ozone-attributable deaths occur at 40-45 ppb while no deaths are due to levels >65 ppb or that there is no discernable pattern for increased/decreased risk depending on concentration. This appears to be an artifact of assuming a linear, no-threshold relationship between mortality and ozone that leads to nonsensical results. In addition, EPA does not include confidence intervals for mortality estimates and therefore fails to demonstrate that any risk reductions calculated for alternative standards are statistically significant.

Results of the APHENA study (Katsouyanni *et al.* 2009) demonstrate that model specifications have significant effects on the results and may even change the interpretation of the findings. This highlights the uncertainties in mortality estimates, which vary substantially in effect size as well as statistical significance across cities depending on modeling choices. Indeed the APHENA authors conclude that there is no single method that is entirely adequate and that seasonal confounding remains an important limitation for the interpretation of this body of literature.

Finally, EPA states on page 7-69 of the HREA that mortality risk is generally not responsive to alternate standards. In other words, the proposed standards would not be expected to have a significant impact on mortality risk. It would then follow that EPA

anticipates that there will be no appreciable benefits expected from the proposed alternative standards for this endpoint. The TCEQ agrees with EPA that lowering the ozone standard will not result in appreciable health benefits.

**The rationale for lower ozone standard is inadequate.**

EPA does not present a clear rationale for the necessity of a lower standard. For instance, the evidence presented by for respiratory endpoints EPA appears to cast doubt on the lower end of the proposed range of alternative standards. In addition, EPA indicates "...a mostly consistent positive association between $O_3$ exposure and respiratory-related hospital admissions and ED visits..." The TCEQ does not believe that "mostly consistent" is strong enough evidence for using these endpoints for setting a lower NAAQS.

The rationale for a lower NAAQS based on mortality data presented by EPA is tenuous. For example, figure 3-16 presents hypothetical risk below 60 ppb. We would like to emphasize that 20 and 40 ppb included in this graph are well below the range of any of the alternative standards under consideration. Moreover, the document argues that the rationale for lowering the NAAQS is on the basis of affects "allowed" to occur under the current standard. These data indicate that the choice of any of the alternative standards under consideration is arbitrary, based on results presented by EPA.

In addition, the three observations on page 3-112 are based on mortality over the full range of ozone concentrations and based on figure 3-16, the choice of a 60—70 ppb standard will not appreciably change any of these key observations. Moreover, the final line of the REA states "[m]ortality from short-term and long-term $O_3$ exposures and respiratory hospitalization risk is not greatly affected by meeting lower standards..." We agree with EPA that the proposed alternate standards will not have an impact on respiratory hospitalization risk, therefore the existing standard should be retained.

Finally, on page 3-115 and elsewhere in discussion of uncertainty related to effects at low concentrations of ozone EPA makes contradictory statements. EPA calculates increases in theoretical mortality resulting from alternative standards leading to potentially substantial disbenefits. However, EPA argues that the decreases in health effects estimated for higher ozone concentrations are real whereas the increases in those same health effects at lower concentrations are uncertain. It can't be both ways. This is the impact of choosing a linear model and calculating risks below LMLs of available studies as well as background and highlights the tenuous connection between the ozone data and the mortality data, especially at concentrations below the present standard.

EPA's own modeling shows either adverse or little to now public health benefit from lowering the current standard, therefore TCEQ urges EPA to retain the existing standard.

**Specific Comments**

- Page 1-23, line 15 – it is not correct to say that multi-city studies "are not prone" to publication bias. It would be more accurate to say "are less prone."

- Page 2-15 - please clarify meaning of "site-days."
- P3-7, line 21 – given the limitations of epidemiological study design, "can result in" should be changed to "may be associated with."
- Page 3-13, line 13 is too vague in saying that "[o]zone exposures result in increased respiratory tract inflammation and epithelial permeability." There should be some indication of the concentrations at which this has been observed.
- Page 3-19 – imprecise description of role of eosinophils in inflammation. More accurate to say that they mediate inflammatory responses and numbers of this cell type are increased in allergic conditions, such as asthma.
- P3-22, line 25 - please provide a citation.
- Page 3-39 – update citation to most recent ATS guidance on adversity.
- P3-60 line 10-12, should read "...individuals *may* experience clinically meaningful decrements..." to accurately reflect uncertainty related to applying the MSS model to a particular population as well as the uncertainty related to the clinical relevance of small decrements in $FEV_1$ alone which are arguably not adverse (ATS 2000).
- Figures 4-1 through 4-4 the same scale should be used.

## REFERENCES


Abbey, DE; Nishino, N; McDonnell, WF; Burchette, RJ; Knutsen, SF; Lawrence Beeson, W; Yang, JX. 1999. "Long-term inhalable particles and other air pollutants related to mortality in nonsmokers." Am J Respir Crit Care Med. 159(2):373-382.

Adams WC. 2002. "Comparison of chamber and face-mask 6.6-hour exposures to ozone on pulmonary function and symptoms responses." Inhal Toxicol. 14(7): 745-764.

Adams WC. 2006. "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(2): 127-136.

American Thoracic Society. 2000. "What constitutes an adverse health effect of air pollution?" Am J Respir Crit Care Med. 161: 665-673.

Beeson, WL; Abbey, DE; Knutsen, SF. 1998. "Long-term concentrations of ambient air pollutants and incident lung cancer in California adults: Results from the AHSMOG study." Environ Health Perspect. 106: 813-823.

Brauer, M; Brumm, J; Vedal, S; Petkau, AJ. 2002. "Exposure misclassification and threshold concentrations in time series analyses of air pollution health effects." Risk Anal. 22: 1183-1193.

Brown, JS. [US EPA]. 2007. Memo to Ozone NAAQS Review Docket (OAR-2005-0172) re: The effects of ozone on lung function at 0.06 ppm in healthy adults. 8p., June 14.

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(8):1023-1026.

Chen, LH; Knutsen, SF; Shavlik, D; Beeson, WL; Petersen, F; Ghamsary, M; Abbey, D. 2005. "The association between fatal coronary heart disease and ambient particulate air pollution: Are females at greater risk?" Environ Health Perspect. 113: 1723-1729.

Dockery DW, Pope CA, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr., Speizer FE. 1993. "An association between air pollution and mortality in six U.S. cities." N Engl J Med. 329(24):1753-1759.

Folinsbee, LJ; McDonnell, WF; Horstman, DH. 1988. "Pulmonary function and symptom responses after 6.6-hour exposure to 0.12 ppm ozone with moderate exercise." J Air Waste Manag Assoc. 38: 28-35.

Geyh, AS; Xue, J; Ozkaynak, H; Spengler, JD. 2000. "The Harvard Southern California chronic ozone exposure study: Assessing ozone exposure of grade-school-age children in two southern California communities." Environ Health Perspect. 108: 265-270.

Goodman, JE; Prueitt, RL; Chandalia, J; Sax, SN. 2013. "Evaluation of adverse human lung function effects in controlled ozone exposure studies." J Appl Toxicol. Jul 9. doi: 10.1002/jat.2905. [Epub ahead of print]

Goodman, JE; Lunch, HN; Zu, K; Sax, SN; Venditti, FJ; Prueitt, RL. 2014. "Weight-of-evidence evaluation of long-term ozone exposure and cardiovascular effects." Submitted.

Jerrett M, Burnett RT, Ma R, Pope CA, Krewski D, Newbold KB, Thurston G, Shi Y, Finkelstein N, Calle EE, Thun MJ. 2005. "Spatial analysis of air pollution and mortality in Los Angeles." Epidemiology. 16(6):727-736.

Jerrett M, Burnett RT, Pope CA, Ito K, Thurston G, Krewski D, Shi Y, Calle E, Thun M. 2009. "Long-term ozone exposure and mortality." N Engl J Med. 360(11):1085-1095.

Katsouyanni, K; Samet, JM. 2009. "Air pollution and health: A European and North American approach (APHENA)." Health Effects Institute. 132p. October 29.

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.

Krewski, D; Burnett, RT; Goldberg, MS; Hoover, K; Siemiatycki, J; Jerrett, M; Abrahamowicz, M; White, WH 2000. "Reanalysis of the Harvard Six Cities study and the American Cancer Society

study of particulate air pollution and mortality." Health Effects Institute. http://pubs.healtheffects.org/view.php?id=6

Lee K, Parkhurst WJ, Xue J, Ozkaynak AH, Neuberg D, Spengler JD. 2004. "Outdoor/Indoor/Personal ozone exposures of children in Nashville, Tennessee." J Air Waste Manag Assoc. 2004 Mar;54(3):352-9.

Lipfert FW, Perry HM, Miller JP, Baty JD, Wyzga RE, Carmody SE. 2000. "The Washington University-EPRI Veterans' Cohort Mortality Study: Preliminary results." Inhal Toxicol. 12(Suppl. 4):41-73.

Lipfert, FW; Baty, JD; Miller, JP; Wyzga, RE. 2006. "PM2.5 constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans." Inhal Toxicol. 18: 645-657.

McDonnell, WF; Kehrl, HR; Abdul-Salaam, S; Ives, PJ; Folinsbee, LJ; Devlin, RB; O'Neil, JJ; Horstman, DH. 1991. "Respiratory response of humans exposed to low levels of ozone for 6.6 hours." Arch. Environ. Occup Health. 46:145-150.

McDonnell, WF; Stewart, PW; Smith, MV; Kim, CS; Schelegle, ES. 2012. "Prediction of ozone-induced lung function responses in humans." Inhal Toxicol. 22(2);160-168.

Meng, Q; Williams, R; Pinto, J.P. 2012. "Determinants of the associations between ambient concentrations and personal exposures to $PM_{2.5}$, $NO_2$, and $O_3$ during DEARS." Atmospheric Environment. 63:109-116.

Miller, KA; Siscovick, DS; Sheppard, L; Shepherd, K; Sullivan, JH; Anderson, GL; Kaufman, JD. 2007. "Long-term exposure to air pollution and incidence of cardiovascular events in women." N Engl J Med. 365 (5):447-58.

O'Connor, GT; Neas, L; Vaughn, B; Kattan, M; Mitchell, H; Crain, EF; III, ER; Gruchalla, R; Morgan, W; Stout, J; Adams, GK; Lippmann, M. 2008. "Acute respiratory health effects of air pollution on children with asthma in US inner cities." J Allergy Clin Immunol. 121: 1133-1139.

O'Neill, MS; Ramirez-Aguilar, M; Meneses-Gonzalez, F; Hernandez-Avila, M; Geyh, AS; Sienra-Monge, JJ; Romieu, I. 2003. "Ozone exposure among Mexico City outdoor workers." J Air Waste Manag Assoc. 53:339-346.

Pope, CA, III; Burnett, RT; Thun, MJ; Calle, EE; Krewski, D; Ito, K; Thurston, GD. 2002. "Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution." JAMA. 287: 1132-1141.

Rhomberg LR, Chandalia JK, Long CM, Goodman JE. 2011. "Measurement error in environmental epidemiology and the shape of exposure-response curves." Crit Rev Toxicol. 41(8):651-671.

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(3):265-272.

Schildcrout, JS; Sheppard, L; Lumley, T; Slaughter, JC; Koenig, JQ; Shapiro, GG. 2006. "Ambient air pollution and asthma exacerbations in children; An eight-city analysis." Am J Epidemiol. 164(5):505-517.

Smith RL, Xu B, Switzer P. 2009. "Reassessing the relationship between ozone and short-term mortality in U.S. urban communities." Inhal Toxicol. 21(Suppl. 2):37-61.

Wang, XY; Hu, W; Tong, S. 2009. "Long-term exposure to gaseous air pollutants and cardio-respiratory mortality in Brisbane, Australia." Geospat Health. 3: 257-263.

Xue, J; McCurdy, T; Spengler, J; Ozkaynak, H. 2004. "Understanding variability in time spent in selected locations for 7-12-year old children. J Expo Anal Environ Epidemiol. 14: 222-233.

Zanobetti A, Schwartz J. 2008. Is there adaptation in the ozone mortality relationship: A multi-city case-crossover analysis." Environ Health. 7:22.