

May 19, 2014

Dr. H. Christopher Frey
Chair, Clean Air Scientific Advisory Committee
Science Advisory Board
US Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460

Re: Draft Letter on the Clean Air Scientific Advisory Committee (CASAC) Review of EPA's *Second Draft Health Risk and Exposure Assessment for the Review of the Ozone National Ambient Air Quality Standards*

Dear Dr. Frey:

In its draft letter to the United States Environmental Protection Agency (EPA) regarding the *Second Draft Health Risk and Exposure Assessment for the Review of the Ozone National Ambient Air Quality Standards*, CASAC identified several important improvements in the risk assessment methodology that EPA employed in the Health Risk and Exposure Assessment (HREA). This includes the use of the Higher-order Decoupled Direct Method (HDDM) to model ozone concentrations in urban areas under scenarios of just meeting the current and lower alternative ozone standards (*i.e.*, 60, 65 and 70 ppb) and the updated McDonnell-Stewart-Smith (MSS) model to estimate lung function effects from ozone exposure. While we agree that these changes improved the HREA, there are several remaining issues that need further consideration.

The HDDM model is a significant improvement over the quadratic rollback method used in the first draft HREA. One major issue, however, is the unquantified uncertainty in ozone concentration estimates and its potential impact on risk estimates. For example, EPA developed ozone sensitivities, or model parameters, to estimate how ozone responds to reductions in NO_x and volatile organic compounds from eight months' worth of 2007 data and applied them to other years (*i.e.*, 2008-2010) to estimate ozone concentrations for meeting current and alternative ozone standards. This approach introduces uncertainty because the estimated sensitivities may not capture ozone reactions under different environmental conditions (*e.g.*, meteorology). CASAC raised concerns about this source of uncertainty, noting that a "low-medium" uncertainty designation may indicate a degree of overconfidence (CASAC, 2014). Given the above considerations, CASAC should ask EPA to clarify how it will interpret the findings in light of this potential uncertainty.

Another improvement in the second draft HREA is the use of the updated MSS model, which incorporates the most recent chamber studies and a threshold option (McDonnell *et al.*, 2012). The MSS model is superior to the previous model used by EPA because it can accommodate many more input parameters and assumptions. However, many of the assumptions and input selections chosen by EPA likely resulted in overestimated risks (which could be zero). In addition, a major limitation of the MSS model is that it does not generate confidence bounds for risk estimates that reflect the uncertainty in the model inputs. In fact, EPA conducted a number of sensitivity analyses and showed that a 5% increase in individual model parameters (such as ventilation rate) resulted in potentially large increases in the number of individuals who would experience > 10% decrements in lung function (*e.g.*, up to a 25% increase for a 5% increase in ventilation rate). For half of the model parameters, a 5% increase in the parameter

increased the population response by at least 5%. CASAC should ask EPA to evaluate the biological plausibility of the changes in estimated effects associated with changes in the model parameters, as this is critical to understanding how reliable the model is.

Uncertainty was also introduced in the MSS lung function modeling when EPA applied the exposure-response functions derived for 18- to 35-year-old adults to children. EPA justified this by noting that evidence suggested that children and adults have similar forced-expiratory-volume-in-one-second (FEV₁) responses to ozone, citing McDonnell *et al.* (1985). In the model, EPA assumed that children were as responsive as 18-year-olds, the most responsive people in the cohort. In sensitivity analyses, EPA showed that when a child's response is set equivalent to the *average* response for the whole cohort (18-35 year olds), the percentage of children with FEV₁ decrements was lower by approximately 2-4%. Given that the scientific evidence does not indicate that children are more responsive than adults (*e.g.*, McDonnell *et al.*, 1985), using an average response as the default for children is a more defensible approach and one that should be used in the core analysis.

With regard to variability, EPA included a variability parameter in the MSS model that is based on a Gaussian distribution, truncated to ± 2 standard deviations. EPA conducted a sensitivity analysis using a distribution that was truncated by the maximum value. This change largely increased the predicted percent of the population that would experience lung function decrements. EPA noted that the assumption that the variability term is Gaussian was convenient but inaccurate. CASAC also raised concerns about this aspect of the modeling, but should follow-up by asking EPA to evaluate the impact of this assumption on the results and whether the results are reliable enough for use in setting the NAAQS.

Similarly, we note that the MSS model performs poorly when predicting individual decrements in FEV₁ (it better predicts the percentage of people above certain FEV₁ values). In addition, determining the percent (or number) of individuals who experience at least one FEV₁ decrement over a cutoff value likely overestimates the significance of individual responses, particularly at lower ozone exposure levels. This is because of the individual variability of FEV₁ when measured by diagnostic spirometry. For example, in a study that took repeated FEV₁ measurements from several healthy individuals exposed to clean air, the observed variation in FEV₁ was up to $\pm 5\%$ in some subjects (Lefohn *et al.*, 2010). This is well within the range of decrements in FEV₁ that was observed in the controlled exposure studies at 60 and 72 ppb. Based on this, a substantial segment of the low-exposed individuals included as responders (*i.e.*, having at least one FEV₁ decrement $> 10\%$) may simply fall within the range of intra-individual variability.

Both the uncertainty and variability call into question whether the small differences in risk estimates between scenarios for just meeting the current standard *vs.* alternative standards are meaningful (*i.e.*, statistically significant). For example, the percentage of children with at least one FEV₁ decrement ($> 10\%$) across all years and cities ranged from 8 to 20% (Table 6-4 in the REA) for a 70 ppb standard scenario, but this was only a few percentage points lower than, and mostly overlapped with, that for the scenario just meeting the current standard (*i.e.*, 11-22%); these *differences* are well within model uncertainty. Results for multiple (≥ 6) days with $>10\%$ FEV₁ decrements, which are more clinically relevant, were much lower, with the percentage of children experiencing FEV₁ decrements ($> 10\%$) ranging from 1 to 6% for the scenario of just meeting the current standard, and only slightly lower with lower standards. Importantly, these differences are the key to the analysis, and they show that meeting alternative standards would not lead to significant, if any, health reductions, given the uncertainty in the models, even for the worst-case scenarios.

Regarding the results based on epidemiology studies, a few comments are warranted. First, CASAC highlighted the mortality estimates as providing meaningful risk reductions with lower ozone standards. This is in contrast to EPA's conclusion regarding the epidemiology studies (US EPA, 2014, p. 7-69). CASAC also did not consider the uncertainty associated with the estimates. The confidence bounds

around these estimates are inclusive of 0, *i.e.*, the data are consistent with no reduction in deaths for most cities. Also, because the confidence bounds overlap within each urban area for alternative lower ozone standards, *differences* between mortality estimates for the current standard *vs.* alternative standards are not statistically significantly different (see Figure 1 below). These are key considerations because they indicate that lowering the ozone standard will not necessarily result in the claimed reductions in mortality, and that there is no real distinctions between meeting the current standard or any of the proposed alternative standards. Furthermore, these confidence bounds do not include all of the model uncertainty, so the actual confidence bounds are likely to be wider than what EPA reported.

CASAC also had questions regarding the analyses of New York City and Los Angeles because of the large NO_x reductions needed to achieve lower ozone standards in these cities. EPA acknowledged that it has far less confidence in the risk estimates for these two cities compared to other cities because drastic NO₂ reductions were needed to achieve alternative ozone standards, causing model instability. Based on the modeling issues in these two cities, CASAC should recommend that the results for these two cities be excluded from consideration when evaluating the risk results, as well as from the summary tables in the executive summary, synthesis chapter, and policy assessment.

In a similar vein, EPA presented mortality risk estimates in heat maps, showing that most of the mortality risk estimates are concentrated in the mid-range of ozone concentrations (~25-55 ppb). This is the range that is most impacted by background ozone concentrations. As noted by CASAC, how background ozone is considered in the interpretation of the risk findings was unclear in the HREA and needs further discussion and clarification.

Overall, there is not a sufficient discussion in the HREA regarding the uncertainty and variability in the modeled health risk estimates that EPA calculated. Importantly, CASAC did not fully discuss how these uncertainties should be considered when interpreting the findings, particularly with regard to small estimated health benefits (that could be zero) from lower standards.

Thank you for your consideration.

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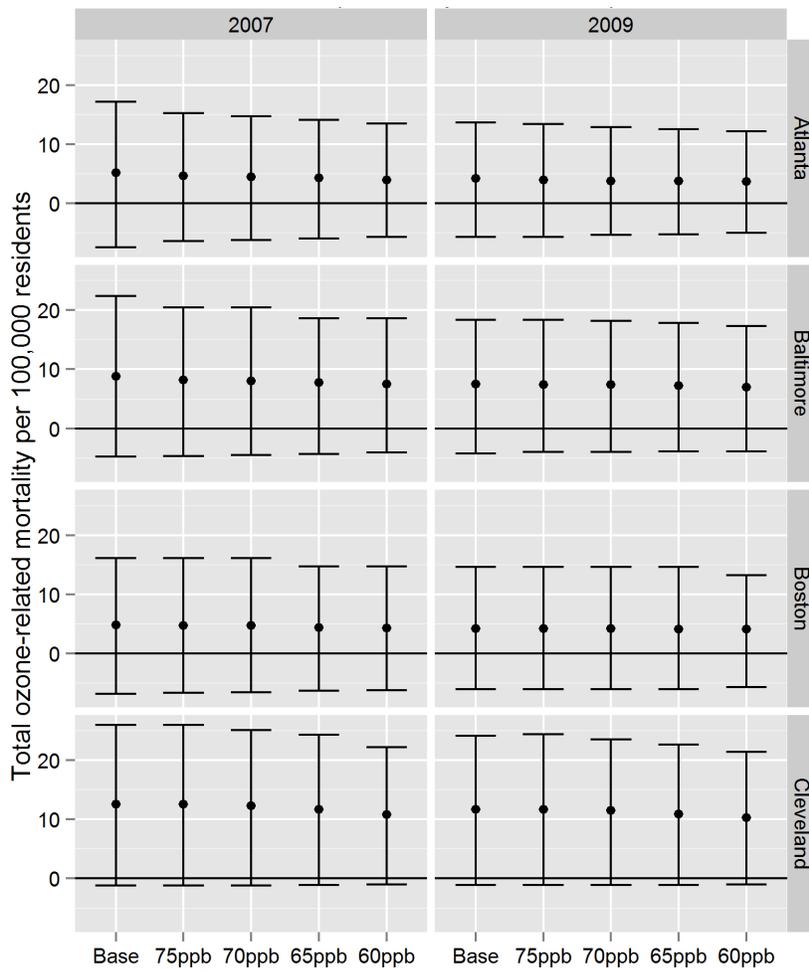


Figure 1 All-cause Mortality Rates (Per 100,000 People) with 95% Confidence Intervals. Mortality rates estimated for air quality meeting base, current, and alternative ozone standard standards in Atlanta, Baltimore, Boston, and Cleveland in 2007 and 2009. Based on the original data in Table 7-7 (US EPA, 2014).

References

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