Follow-up Comments Prepared for the

Clean Air Scientific Advisory Committee
Ozone Review Panel
Public Meeting

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Follow-up Comments on EPA’s Health Risk and Exposure Assessment for Ozone
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At the CASAC Ozone Review Panel Public Meeting on 3/25/2014 - 3/27/2014, CASAC panelists asked some public presenters to identify further research or improvements to the HREA or PA that could be accomplished in a timely manner for consideration during this rulemaking. The following additional comment refers to use of the McDonnell-Stewart-Smith (MSS) model in APEX to provide risk estimates for the numbers of individuals expected to experience FEV₁ decrements under various regulatory scenarios. I propose an additional sensitivity analysis that further elucidates the role that estimation of within-individual variability plays in risk estimates generated by APEX.

In my original written comment #19 to CASAC, I discussed the role of selection of a value of ε (within-individual variability) from the distribution of possible values of ε in the simulation of FEV₁ decrements. In the 2012 MSS model (McDonnell et al., 2012) used for the current HREA, the variance of ε was assumed to be normally distributed and constant for all levels of exposure and was estimated from the model fit. To generate predictions of FEV₁ response for simulated exposures, a value of ε is selected from the distribution of possible values once a day for each individual exposed and added to the individual predicted central tendency of response. Because the estimated variance of ε is rather large (17.1, SD = 4.1) relative to a 10% FEV₁ decrement, the probability that an individual will experience a 10% FEV₁ decrement is quite sensitive to the value of ε selected. EPA has decided, based on conventions previously used in APEX, to truncate the possible values of ε at +/- 2 standard deviations from its mean of zero (+/- 8.27) to reduce the sensitivity of results to extreme values of ε. This should reduce the proportions of individuals with low level exposures (and possibly higher level exposures) experiencing FEV₁ effects, consistent with the results of Table 6F-4 of Appendix 6F.

In a more recent paper (McDonnell et al., 2013) we reasoned that within-subject variability should not be constant but is more likely to be related to magnitude of predicted effect. We refit the MSS model using a new variance structure in which the variance of ε was assumed to be related to the magnitude of predicted central tendency of
individual response. This model fit the data better than the original model that assumed constant variance (although predicted population responses in the original data set were very similar for both models probably because of the shifts observed in other coefficients). The estimated within-individual variance of response for exposures below threshold was 9.1 in the new model rather than the constant 17.1 in the previous model. This value of 9.1 was consistent with the variance of observed responses for below threshold exposures. The level at which ε is truncated in the HREA (+/-8.27) is close to 3 standard deviations from the mean for low-level exposures as estimated in the new model. For exposures and individuals with small predicted responses, the smaller selected values of ε for low level exposures result in more precise estimates of FEV1 decrement for each individual and therefore more accurate estimates of the proportion experiencing a 10% FEV1 change. In the new model the predicted variance of ε increases with increasing predicted response. We have not explored the effect of increasing variance in ε on predicted response for exposures with higher predicted responses nor is it clear how truncation would affect predicted responses at higher levels of exposure.

I would like to suggest that additional sensitivity analyses be conducted using values of ε selected from the distributions estimated in the MSS 2013 paper. The results of these analyses could be compared with existing sensitivity analyses presented in Tables 6F-3 and 6F-4 of Appendix 6F. Because it is unlikely that ε is perfectly normally distributed as the MSS model assumes and because we know that ε includes some noise in addition to true within-individual variability of response, it may also make sense to examine the effect of truncating the distributions of ε estimated in the 2013 paper.
REFERENCES
