

Comments on the CASAC Particulate Matter Review Panel Draft Letter on the *Policy Assessment for the Review of Particulate Matter National Ambient Air Quality Standards—Second External Review Draft (June 2010)*
Fr. Doc. 2010–19415

**Julie E. Goodman, PhD, DABT, Gradient
on behalf of the American Petroleum Institute
August 25, 2010**

Thank you for the opportunity to speak today regarding the 2010 PM Policy Assessment (PA). In the PA, US EPA considers several semi-ecological studies of PM_{2.5} and health effects that rely on either traditional or flexible Cox proportional hazard (PH) models to estimate concentration-response (C-R) associations and calculate risks. At the last CASAC meeting, questions were raised regarding whether the use of Cox PH models is appropriate. I will now describe how the underlying assumptions of the traditional Cox PH model are not always met in PM studies, which could lead to biased risk estimates. While flexible Cox PH models used in other PM studies are not dependent on these assumptions, they are dependent upon parameter specification. There is currently no standardized method for determining which parameters are most appropriate, and models that fit the data equally well can have different shapes and result in different risk estimates.

The traditional Cox PH model is based on two main assumptions. In several studies relied on in the PM ISA and PA, these assumptions are violated.

- The first is that the effects of the exposure and other covariates on the hazard are constant over the study period. In fact, it is far more likely that at least some of the impacts of exposure and other potential confounders vary over time. For example, this has been shown to be the case for the effects of smoking on cardiovascular mortality.
- The second is that exposure and other covariates contribute linearly to the natural log of the hazard ratio. One notable example is body mass index (BMI). BMI can be a confounder of the PM_{2.5} exposure/mortality association and has been shown to contribute nonlinearly to mortality risk.

Overall, the validity of the assumptions of the Cox PH model were not systematically tested in studies relied on by US EPA, and the impacts of potential violations have not been systematically assessed, meaning they could lead to biased C-R curves and resultant risk estimates.

Several researchers have developed a new Cox PH model to more accurately describe real-world data. This model offers added flexibility and does not require the standard assumptions of the original Cox PH model, but this comes at the cost of a more complicated model. Also, flexible Cox PH models

and risk estimates based on them are dependent upon parameter and model specification. Estimates of both nonlinearity and time-dependence can vary depending upon the degrees of freedom and other parameters, and models that fit the data equally well can have different shapes and result in different risk estimates. Although a few methods have been suggested to choose the most appropriate model parameters, none have been systematically assessed, so one cannot know with certainty which risk estimates are most reflective of actual risk.

In conclusion, at this time, in this review, CASAC should recommend that the administrator does not change the PM NAAQS. In the next review cycle, US EPA should address whether the over-reliance on studies that do not verify model assumptions, or do not require those assumptions, lead to biased C-R functions, particularly at low exposure concentrations.