

Oral Testimony Before the CASAC Ozone Review Panel on the Third Draft Ozone ISA and First Draft Ozone REA

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Thank you for the opportunity to speak on behalf of the American Forest and Paper Association. I will be focusing on two issues today: the weight of evidence for cardiovascular effects associated with ozone in the ISA (US EPA, 2012a), and use of the McDonnell *et al.* (2012) model for the risk assessment based on controlled exposure studies in the REA (US EPA, 2012b).

We agree with EPA that the weight of evidence across all available data, including experimental and observational data, is not sufficient to assign a "likely to be causal" classification for cardiovascular effects from short- or long-term ozone exposures because of lack of coherence across the science and weak biological plausibility. There is only suggestive evidence from animal studies of pre-morbidity effects, and this is at levels well above the current ozone standard. The evidence of an association between ozone exposure and cardiovascular mortality is limited and not consistent among epidemiology studies.

CASAC has identified the Devlin *et al.* (2012) study as providing added support for a "likely to be causal" classification. This single study does not provide sufficient support, especially given several issues that should be considered when interpreting its results. For example, Devlin *et al.* (2012) evaluated several biomarkers of inflammation, thrombosis, and HRV that may not be indicative of adverse cardiovascular effects but, rather, indicative of non-adverse homeostatic processes (Goodman *et al.*, 2010). Small changes in HRV are normal and can occur as a result of lifestyle factors (*e.g.*, Felber Dietrich *et al.*, 2006). Only a small proportion of the biomarkers evaluated changed at some point after exposure. If ozone causes cardiovascular effects, consistent changes in biomarkers would be expected, not only changes in a select few biomarkers or at certain times and not others. While it is possible that the mode of action for ozone acts only through a subset of biomarkers at certain time points, Devlin *et al.* (2012) provided no evidence to support this.

In addition, Devlin *et al.* (2012) only evaluated one exposure level, 300 ppb, which is four times higher than the current ozone NAAQS. The use of a single exposure level means that exposure-response, which is critical for addressing causation, could not be addressed. Also, based on known biological modes of action, there is no evidence that small biomarker changes at high exposures indicate the same changes would occur at lower exposures, much less that they would be adverse. Thus, the relevance of the results of this study to current ambient levels cannot be determined.

Finally, it is notable that study subjects were exercising at high multiples of normal breathing levels, resulting in a significant group decrease in pulmonary function – as expected based on previous studies. Other studies using ozone exposure regimens that likely produced a lower pulmonary response have not reported changes in HRV (*e.g.*, Fakhri *et al.*, 2009).

As to my second point, we agree with CASAC that EPA should use the McDonnell *et al.* (2012) model in the next draft REA. This model includes an expanded dataset as well as the option to include a threshold. It is our understanding that the underlying data may not be available for this model, but this should not prevent its use by EPA. EPA did not rely on underlying data when using concentration-response functions from published epidemiology studies.

EPA should calculate actual FEV₁ decrements, rather than the percentage of people with lung function decrements over a certain value (*i.e.*, 10, 15, or 20%), in the exposure-response model. The current approach is inappropriate because it overestimates the significance of individual responses, particularly at lower ozone exposure levels. Because there is only one measurement per person at each exposure level, the results are only informative regarding group responses.

In summary, CASAC should support EPA's conclusion that there is only suggestive evidence of cardiovascular effects associated with short- and long-term ozone exposure. In addition, we agree with CASAC's endorsement of the use of the McDonnell *et al.* (2012) model with the threshold option in the next draft REA, but EPA should use the model to calculate actual FEV₁ decrements, rather than the percentage of people above an FEV₁ cutoff.

On behalf of American Forest and Paper Association, thank you for your consideration of these comments.

References

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