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 Policy 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 Policy Assessment for the Review of the Ozone National Ambient Air Quality Standards (PA)*, CASAC identified several important issues that we agree need further consideration. There are other major points in the letter, however, that we disagree with.

We urge CASAC to inform the Administrator about key findings as well as uncertainties and limitations of the current scientific body of evidence, that bear on the PA. This includes the role of background ozone in calculations of health benefits in the Health Risk and Exposure Assessment (HREA), the many conservative assumptions in the HREA analyses that likely exaggerate health benefits resulting from more stringent standards, and the scientific evidence that indicates that children are not more susceptible to ozone than adults. We discussed these issues in detail in comments provided to CASAC prior to the March 2014 meeting (Goodman and Sax, 2014a,b) and briefly summarize them below.

Background Ozone

Regarding background ozone, CASAC noted that the PA did not clearly discuss how background should be considered in setting the ozone primary and secondary standards. CASAC panel members indicated that methods for calculating background needed to be described in the PA and that the uncertainties needed to be discussed. Specifically, CASAC requested the source apportionment methodology be moved to an appendix and that the zero-out approach be clarified, as CASAC concluded that EPA presented this approach incorrectly (*i.e.*, background is presented as a percent contribution of total ozone, when it should be presented as a "ratio" between modeled background and a base case scenario). Importantly, the PA is missing any discussion of how background could impact meeting an ozone standard (particularly at the lower end of the proposed range) and whether this impact varies by region. This is a major concern because, according to EPA's models, background contributions presented in the PA are large in most areas that were modeled. Also, the lower end of the proposed ozone standard range (*i.e.*, 60 ppb) is close to background levels in parts of the US. This is very important because any health effects associated with background levels cannot be regulated (Lin *et al*., 2012).

In addition, the models EPA used in the HREA indicate that at low ozone levels, reducing NO_2 levels results in higher ozone concentrations, with larger modeled health impacts, particularly in urban areas (US EPA, 2014). These are undesirable outcomes. Moreover, since the health impacts are observed to occur largely in the range of background ozone levels, they are likely to be unavoidable.

CASAC also concluded that the impact of the international transport of air pollutants on ozone concentrations can be quite significant. This was a comment separate from the main letter on the PA, and CASAC simply urged EPA to find a way to solve this by seeking international cooperation. However, the more important issue is how international contributions in combination with naturally-occurring background ozone (*e.g.*, from biogenics or stratospheric-tropospheric exchange), which is much greater, should be considered when setting the ozone standard. Overall, it appears these issues have not been resolved to the satisfaction of CASAC members and need further attention and clarification by EPA.

Adequacy of Primary Standard

CASAC noted that there is "scientifically sound information" for health impacts of ozone in major categories, including lung function decrements, pulmonary inflammation, respiratory symptoms, and respiratory morbidity and mortality. CASAC stated that EPA has reasonably argued that this information calls into question the level of the current standard. Specifically, in response to charge questions for Chapter 4, the draft CASAC letter stated:

> CASAC concurs that 60 ppb is an appropriate and justifiable scientifically based lower bound for a revised primary standard. This is based upon findings of adverse effects, including clinically significant lung function decrements and airway inflammation, after exposures to 60 ppb ozone in healthy adults with moderate exertion (Adams 2006; Schelegle *et al.* 2009; Brown, 2008; Kim *et al*., 2011), with limited evidence of adverse effects below 60 ppb. (CASAC, 2014)

We note that the scientific evidence is equivocal at ozone levels below the current standard of 75 ppb. Controlled exposure studies are limited, and few have shown any effects below the current standard. Goodman *et al*. (2013) reviewed the controlled exposure literature and found that adverse effects (*i.e.*, moderate lung function decrements accompanied by respiratory symptoms) were only observed at exposures above the current ozone standard. As discussed in detail in our previous comments, only Schelegle *et al*. (2009) reported statistically significant, but small, FEV_1 decrements at 72 ppb (Goodman and Sax, 2014a,b). Importantly, these decrements are not considered to be adverse or clinically significant according to ATS criteria (ATS, 2000). Other studies have reported even smaller lung function decrements at 60 ppb that were statistically significant only because a questionable statistical approach was used (*i.e.*, a majority of pertinent data were excluded in the analysis), and the decrements were not associated with concomitant respiratory symptoms (Kim *et al*., 2011; Brown *et al*., 2008). Therefore, these decrements should not be considered adverse or clinically significant.

In addition to respiratory decrements and symptoms, pulmonary inflammation has been cited as a possible justification for lowering the current ozone standard. However, only one controlled exposure study (*i.e.*, Kim *et al*., 2011) reported statistically significant differences in pulmonary inflammatory markers, and these are not likely clinically significant. Thus, this particular study provided insufficient evidence to conclude effects below the current standard. Studies evaluating higher ozone concentrations and inflammatory markers have been mixed. In one study there was no concentration-response between ozone exposures for one hour to 125-250 ppb and inflammatory markers in healthy subjects (Holz *et al*., 1999), while in a meta-analysis of controlled exposure studies of ozone exposures (80-600 ppb) and inflammatory markers there was a linear trend for exposure from 80-600 ppb ozone (Mudway and Kelly, 2004). Animal studies only report inflammatory effects at exposure levels well above the current standard (US EPA, 2013). Findings from epidemiology studies are mixed, with some studies reporting statistically significant changes in inflammatory markers and others reporting no changes (US EPA, 2013, *e.g.*, Figure 6-11). The limitations of the epidemiology studies (*e.g.*, exposure measurement error and confounding) make these studies difficult to interpret, particularly for setting an ozone standard. The very

limited evidence of clinically significant pulmonary inflammation at exposures below the current standard (*i.e.*, a single study) and mixed evidence at higher ozone levels, is insufficient to support lowering the standard.

Susceptible Populations

The CASAC letter also raised the question of susceptible population groups, stating:

> The CASAC further notes that clinical studies do not address sensitive subgroups, such as children with asthma, and that there is a scientific basis to anticipate that the adverse effects for such subgroups are likely to be more significant at 60 ppb than for healthy adults. (CASAC, 2014)

Quite the contrary, the current state of science does not support more significant effects in susceptible population groups. This is discussed in more detail in previous comments (Goodman and Sax, 2014a,b). Briefly, as discussed by Dr. Vedal, one of the largest multicity studies of 861 asthmatic children in the US found little evidence of FEV_1 decrements or asthma-related symptoms with exposures to ozone (O'Connor *et al*., 2008). Similarly, the Children's Health Study, the largest cohort study of children, has consistently reported no respiratory effects associated with ozone, including asthma (*e.g.*, Peters *et al*., 1999; Gauderman *et al*., 2000, 2002, 2004; McConnell *et al*., 2002, 2010; Berhane *et al*., 2004). These studies were largely ignored in the PA. CASAC should urge EPA to include a detailed discussion of these studies, and how they bear on evidence for ozone health effects, before providing a recommendation to the Administrator.

Uncertainties and Data Gaps

Finally, CASAC identified major uncertainties and data gaps that need to be addressed for future reviews, including exposure-response functions, identification of an ozone threshold, the contribution of co-pollutants and temperature, model specification issues, information on health effects of at-risk populations, time-activity data, and characterizing the contribution of background ozone to adverse health outcomes. We agree these are key issues that have not been resolved. Importantly, these issues bear on the interpretation of the *current* scientific literature on ozone health effects, particularly the epidemiology literature. CASAC should ask EPA to clarify how it will interpret the epidemiology literature in light of all of the important sources of uncertainty identified in the CASAC letter. We conclude that they call into question the health effects findings from *current* epidemiology studies, and that these studies do not provide sufficient scientific justification for lowering the current standard.

Taken together, current scientific evidence on ozone health effects from controlled exposure, epidemiology, and experimental animal studies do not support lowering the ozone standard. Therefore, we urge CASAC to recommend that 75 ppb be included in the range of options presented to the Administrator.

Thank you for your consideration.

Sincerely,

GRADIENT

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