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[redacted]

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Grace Appelbe
Legislative Clerk
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515
Email: grace.appelbe@mail.house.gov

RE: H.R. 806, Ozone Standards Implementation Act of 2017 – further questions and responses

Dear Ms. Appelbe,

Please find below my answers to the further questions of Hon. John Shimkus and Hon. Frank Pallone, Jr.

Sincerely,

[redacted]

Homer A. Boushey, M.D.

Responses to questions from the Honorable John Shimkus:

1. **Is there a high degree of variability in individual performance on lung function tests from day-to-day and season-to-season?**

Yes, there is variability in even a healthy individual's performance on pulmonary function testing performed correctly on consecutive days. For the most commonly used measures, the forced expired volume in one second and the forced vital capacity, the values vary by about ±2.5 - 5.0%. That is different, however, from the variability in the mean values for a group of subjects measured on consecutive days over time, or before and after an intervention. So, for example, a decline in FEV1 of 2.5% after ozone exposure in an individual might simply reflect the natural "wobble" of the test. However, the same change in the mean value for FEV1 in a group of subjects would have greater significance, indicating a true effect of the exposure.

a. **What are the factors unrelated to asthma that can affect performance?**

Factors unrelated to asthma that can affect performance of the test are other lung diseases, like chronic obstructive pulmonary disease (COPD, i.e., emphysema and chronic bronchitis), acute bronchitis, cystic

fibrosis, tracheomalacia, vocal cord dysfunction, and others. The test can be affected as well by obesity, weakness, chest wall deformity, and other mechanical problems of the skeletal and neuromuscular function. These, however, are usually recognizable when the test is performed or from the pattern of the curves of expiratory flow, typically displayed along with the test results.

b. **How common is it for clinicians to arrive at different diagnoses for people who present asthma symptoms?**

The frequency with which symptoms of asthma are misdiagnosed as due to another illness varies by the population in which they occur. Asthma is probably over-diagnosed in children under 6 year of age, where wheezing can be caused by viral respiratory infection in the absence of asthma. It is likely under-diagnosed in older patients, in whom wheezing may be mis-attributed to COPD. Among patients between the ages of 6 and 60 years of age, however, the cluster of typical symptoms, abnormal pulmonary function tests, and the coincidence of evidence of allergy make the diagnosis pretty straight-forward.

c. **What other illnesses or conditions could affect lung function performance?**

Please see response to question 1a, above.

2. **In your testimony, you also cite studies by Schelegle et. al. and Kim et al. as affirming lung function decrements in healthy adults after exposure to 60 to 70 ppb of ozone. The studies reported average lung function FEV1 (forced expiratory volume in 1 second) deficits of3.5 and 1.7 percent respectively. In 2005 the American Thoracic Society and the European Respiratory Society (ATS/ERS) issued a paper (Pellegrino et al.)1 to provide guidance in interpreting pulmonary function tests. This paper notes: "When using per cent change from baseline as the criterion, most authorities require a 12-15% increase in FEV1 and/or FVC as necessary to define a meaningful response. Increments of 8% (or ,150 mL) are likely to be within measurement variability [107, 115]." It also notes: "Thus, in subjects with relatively "normal" lung function, year-to-year changes in FEV1 over 1 yr should exceed 15% before confidence can be given to the opinion that a clinically meaningful change has occurred [5]."**

   a. **Please explain the significance of the mean responses found in the Schelegle et al. and Kim et al. studies in light of the ATS/ERS guidance.**

The ATS/ERS statement refers to changes in an individual patient, not to changes in the mean value of a group of subjects measured before and after an experimental exposure to ozone (please see response to question 1, above).

3. **You state in your testimony that a recent publication by Gauderman and colleagues 2 "demonstrated improvements in lung-function development in children as air quality improved." However, the study authors state that "[C]hanges in ozone (Figure 2)) and PM10 PM2.5 (Fig. S4 in the Supplementary Appendix) were not associated with differences in mean FEV1 or PVC values at 11 or 15 years of age or**

with 4-year growth in these values." The study also notes that the evidence regarding the long-term effect of ozone on children is mixed: "Only a few other studies have addressed the long-term effects of ozone on lung function in children, and the results have been inconsistent."

a. **Please explain the significance of the Gauderman study to legislation addressing ozone regulations.**

The remarkable finding reported by Gauderman et al. is that of improvement in pulmonary function in three large cohorts of children in southern California recruited over consecutive periods in which air pollution improved (1993, 1997, and 2003). They demonstrated an association between improvements in air quality, especially in nitrogen dioxide and particulate matter (PM2.5) and increases in lung function growth. The demonstration of a statistically significant association does not prove causality, of course, but the data reported are consistent with the findings of other studies showing improvements in lung function in children who moved from areas with polluted air to areas with less air pollution. Because impairments in lung function in childhood are predictors of chronic respiratory and cardiovascular disease, these findings are heartening evidence of the value of protection of air quality as a public health measure. Gauderman's study did not find an association between reductions in ozone levels and improvements in lung function, but since tail-pipe emissions are the major source of nitrogen dioxide, ozone, and particulate matter in southern California, the measures to reduce ozone (which did decrease, though modestly, over the study periods) contributed to the reductions in nitrogenous products and particulates as well.

4. **You note in your testimony the results of one study by Rice et al. that reported lower FEV1 values in a cohort of generally healthy adults after days of ambient exposure to ozone under 59 parts per billion (ppb), compared to exposures that ranged from 59 to 74 ppb. The study by Rice et al., however, also states that: "The magnitude of the average difference in FEV1 between "good" and "moderate" exposures is small (20 ml for PM2.5, 31 ml for NO_2, and 56 ml for O_3) and unlikely to be clinically perceptible to the average individual."**

a. **Please explain whether you agree with that statement.**

The declines in mean values of pulmonary function after relatively brief exposures of a group of healthy subjects to ozone indicate a true effect. We know from prior studies that these effects of ozone exposure are associated with lung inflammation. The changes themselves may not have been associated with symptoms noticeable to the study participants over the short term, but repeated exposure, and repeated inflammatory insult to the lungs over time, appear to result in accelerated loss of lung function in adults, and in increased likelihood of development of asthma and reductions in lung growth in children.

Responses to questions from the Honorable Frank Pallone, Jr.:

1. **Dr. Boushey, although the title of this bill suggests that it deals only with ozone, in fact it amends the National Ambient Air Quality Standards program of the Clean Air Act for all criteria air pollutants - lead, sulfur dioxide, nitrogen oxides, carbon**

monoxide, and for both fine and course particulate matter. Of course, when we breathe the surrounding air we get any and all of these air pollutants that are in the immediate area. And, while each of them presents different specific health impacts, taken together I imagine they make a very unhealthy brew.

a. **Is it possible we are underestimating the impacts of ozone or other individual pollutants because of the challenge of evaluating and quantifying the cumulative impacts of the mixture of pollutants that people actually are exposed to?**

The thrust of this question is correct - that what research scientists have generally attempted to assess is the independent effect of each criteria pollutant, whereas what people inhale in day-to-day life is the mix of pollutants present in ambient air. It is much harder to assess the effects of complex mixes of pollutants in exposure studies, and it is entirely possible that the effects of a mix of pollutants is greater than the sum of their individual effects. This may indeed account for the consistency of epidemiologic studies showing an increase in asthma exacerbations requiring emergency room treatment to be associated with increases in the ozone levels in "summer fog" – a mix of ozone, nitrogen oxides, sulfates, and particulate matter – when controlled exposures to the same levels of ozone do not induce exacerbations in asthmatic volunteers. There is also an enlarging body of evidence that shows associations between exposure to the traffic mixture of emissions and asthma exacerbations.

2. **Unfortunately, California's topography and climate create conditions that are truly challenging for improving air quality. But, as I understand it the current ozone standard of 70 parts per million, even when we achieve it, may still result in health impacts. Is that true? Did the Clean Air Scientific Advisory Committee and the public health community recommend a stronger standard?**

Congressman Pallone is correct. Health impacts from ozone exposure will occur even with exposure to 70 ppb. This is why the Clean Air Scientific Advisory Committee recommended a new standard of between 60 and 70 ppb, a recommendation widely supported in the public health community (see R. Dey et al., *American Journal of Respiratory and Critical Care Medicine*, 2010; 181:297-299).

3. **Even the extreme non-attainment areas are going to have until 2036 or 37 to achieve compliance with the 70 parts per million ozone standard. So, a child born today in areas with high ozone levels will be 20 years old by the time we achieve compliance with this standard. Doesn't a life- time exposure to air pollution carry a significant health cost for these individuals?**

Again, the Congressman is correct. The evidence suggests that exposure to ozone and other air pollutants impairs lung growth in children, and reductions in pulmonary function at the end of childhood are associated with higher risk of chronic respiratory and cardiovascular disease (see DW Dockery and JH Ware, *New England Journal of Medicine*, 2015; 372:970-972)