Comments on the US EPA's Integrated Science Assessment for Ozone (External Review Draft) Docket # EPA-HQ-ORD-2018-0274

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Thank you for the opportunity to speak today. I am speaking on behalf of Gradient, but my time spent preparing these comments and calling into this meeting has been supported by the American Petroleum Institute.

The 2019 draft Ozone ISA includes new details on the literature search and study selection, including links to view a database of the studies included in the ISA and some brief information on study quality. In addition, it is encouraging to see that biological plausibility assessments play a larger role than they have in the past.

However, several issues still remain. Study quality information is limited and presented in an unclear manner on the online database, and in the draft Ozone ISA, study quality is not fully or consistently considered. Furthermore, while the draft Ozone ISA emphasizes biological plausibility for each health outcome with regard to ozone exposure, the evidence presented does not demonstrate a complete pathway connecting ambient ozone exposure to downstream health endpoints.

The NAAQS systematic review and casual determination framework should be updated to allow for conclusions that are reflective of the weight of scientific evidence, and this framework should be followed and described in a transparent manner in the ISA. I note that suggestions for an updated framework are described in Gradient's written comments on the draft Ozone ISA.

The evidence for respiratory effects does not support EPA's conclusion that there is a causal relationship between short- or long-term ozone exposure and respiratory morbidity and mortality at relevant concentrations. The controlled human exposure studies indicate that there are no statistically significant adverse respiratory effects associated with ozone exposures below 70 ppb. Effects reported at 60 ppb are also not adverse. In addition, the 2013 Ozone ISA did not properly consider key limitations in the epidemiology evidence, and new studies have the same critical issues of that impact the validity of the results. Furthermore, key toxicity studies on which EPA relied to support the epidemiology data were conducted at very high exposure levels that are not relevant for assessing health effects of ambient ozone.

The evidence for metabolic effects does not support EPA's conclusion that there is a likely causal relationship between such effects and short- and long-term ozone exposure at relevant concentrations. The draft Ozone ISA acknowledges that there is limited evidence from epidemiology and controlled human exposure studies, but indicates that animal toxicity studies provide robust evidence of the effects of short-term ozone exposure on metabolic effects. While key animal toxicity studies may support the effects of short-term ozone on glucose impairment at 500-1,000 ppb, the evidence for other metabolic endpoints is not consistent, and many studies only evaluate ozone exposure concentrations that are far higher than ambient levels. Also, animal toxicity and human epidemiology studies are limited regarding long-term effects of ozone on metabolic endpoints. Overall, the evidence presented is inadequate to assign causation between ozone and metabolic effects in humans.

As indicated in the 2019 draft Ozone ISA, evidence for short-term ozone exposure and cardiovascular effects and total mortality certainly does not support a likely causal relationship. However, it also is not suggestive of a causal relationship; rather, it remains inadequate to address causality, if not suggestive of a

lack of association. Finally, I concur with the draft Ozone ISA that the evidence for other endpoints does not support causal or likely causal associations; however, like the evidence for short-term ozone exposure and cardiovascular effects and total mortality, this evidence falls short of suggestive.

In conclusion, the draft Ozone ISA has adopted several important aspects of systematic review that have been absent in prior ISAs. However, it is still not fully transparent, and it does not adequately take study quality or relevance into consideration. Taken together, the currently available science does not provide evidence that supports health effects at ozone concentrations below the current primary standard.