Comments on the Risk and Exposure Assessment to Support the Review of the SO_2 Primary National Ambient Air Quality Standards: Second Draft

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The Risk and Exposure Assessment (REA) to Support the Review of the SO_2 Primary National Ambient Air Quality Standard (NAAQS) suggests a 1-hour daily maximum SO_2 standard within a range of 50 to 150 ppb. This is based primarily on human clinical studies of exercising mild-to-moderate asthmatics and secondarily on epidemiology evidence (US EPA, 2009). As I will discuss over the next few minutes, this range is *not* appropriate because human clinical studies of exercising mild-to-moderate asthmatics show no statistically significant increase of respiratory symptoms at SO_2 peak exposures < 400 ppb, and also because epidemiological studies do not provide supportive evidence.

The dose-response profile for short-term SO_2 exposure has remained relatively consistent over the years. The lowest short-term SO_2 exposure with significant pulmonary function deficits is 400 ppb, at which some individuals have respiratory symptoms but there is high interindividual variability. At 600 to 1,000 ppb SO_2, respiratory symptoms are more consistent, but diminish after cessation of exercise. This is exemplified in Table 5-1 of the SO_x ISA (US EPA, 2008), which states:

- At 1 to 10 minutes at 400 ppb, "Moderate or greater decrements in lung function clearly demonstrated in asthmatics during exercise with significant interindividual variability in response…. Respiratory symptoms … observed at concentrations as low as 0.4 ppm."
- At 1 to 10 min at 600 ppb, "Clear and consistent SO_2-induced increases in respiratory symptoms observed … Respiratory effects attributed to SO_2 among asthmatics during exercise may be diminished after cessation of exercise, even with continued SO_2 exposure."

The SO_2 ISA also states that there is "limited evidence of SO_2-induced increases in respiratory symptoms" at 5 to 10 minutes at 200 ppb, but this is not the case. There is no evidence of statistically significant SO_2-induced increases in respiratory symptoms at peak exposures < 400 ppm. NAAQS are not intended to prevent any biological effect, but rather to be protective against *adverse* effects. A transient decrement in lung function should not automatically be considered an adverse effect. In fact,

minor transient lung function changes are observed in exercising controls and can be induced by other stimuli such as cold, dry air, stress, and fatigue.

The SO_2 REA defines a "moderate or greater lung function decrement" as ≥ 100% increase in sRaw or ≥ 15% decrease in FEV_1. Figures 4-2 and 4-3 of the SO_2 ISA clearly show that these effects do not appear until 10-minute SO_2 exposures in *sensitive* asthmatics reach 400 ppb. The SO_2 REA calls attention to decrements in lung function occurring in 5 to 30% of exercising asthmatics exposed to 200 to 300 ppb SO_2 for 5-10 minutes, but neglects to discuss that these effects are not big enough to be considered adverse, by their own definition, nor are they statistically significant. Still, the REA also states that "it is likely that a percentage of asthmatics would also experience bronchoconstriction following exposure to levels lower than 200 ppb." Given that neither adverse nor statistically significant effects occur until exposures of 400 ppb and above, it is highly unlikely that asthmatics would experience adverse effects, according to the REA definition, at exposures < 200 ppb.

Clinical studies of SO_2 assessed sensitive individuals. In clinical studies of SO_2, subjects were mostly mild and moderate asthmatics at exercise and included both adolescent and adult asthmatics at exercise. In addition, asthmatic adolescents were exposed *via* mouthpiece, which resulted in them receiving higher SO_2 exposures than in "real world" scenarios. Linn et al. (1987) found responses of moderate/severe asthmatics to increasing SO_2 concentrations were roughly similar to those of minimal/mild asthmatics, suggesting that results of these studies are applicable to severe asthmatics.

The clinical studies assessed rare events in sensitive individuals that do not represent typical real-world scenarios. Unmedicated asthmatics are unlikely to be engaged in moderate exercise. It is even more unlikely that unmedicated asthmatics or other sensitive individuals would exercise near a SO_2 source that has the potential to produce high ground-level SO_2 concentrations. Also, if peak short-term SO_2 exposures ranged from 600 to 1,000 ppb, respiratory effects would likely be diminished by cessation of exercise, even if high SO_2 exposures persisted.

With regard to the epidemiology data as a whole, studies do not support the REA's suggested 1-hour daily maximum. The majority of epidemiology studies reported null or weakly positive findings, and weakly positive findings often became non-significant when adjusted for co-pollutants. Moreover, information on co-pollutants or other exposure-related factors was not included in many studies. It is possible that exposure misclassification biased results in either direction. In addition, measurements from

central monitors, which were used to determine exposures in the majority of epidemiology studies, are not representative of human exposure and may have also led to biased results. It is notable that epidemiology findings are inconsistent with better-controlled human clinical studies.

All risk estimates calculated in epidemiology studies are very small, and are near null if not actually null. Exposure misclassification and known, residual, unmeasured and/or unknown confounders likely biased risk estimates away from the null. As stated in the REA, "only a limited subset of these studies investigated potential confounding by co-pollutants" and "inclusion of PM_{10} in multi-pollutant models often resulted in the SO_2 effect estimate losing statistical significance."

In conclusion, clinical data do not support the suggested 1-hour daily max SO_2 NAAQS. These studies include sensitive individuals (*e.g.*, asthmatic adults and adolescents), examine a rare event in which, if symptoms occur, they can be relieved by discontinuing exercise. The effects that occur at exposures < 400 ppb do not meet REA's definition of adverse and are not statistically significant. Thus, the use of these data makes the use of safety factors for sensitive individuals, non-human data, use of a LOAEL, and use of chronic exposures unnecessary. Owing to their many limitations, epidemiology studies also do not support the suggested 1-hour daily max SO_2.

References

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