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regarding

Risk and Exposure Assessment to  
Support the Review of the SO<sub>2</sub> Primary  
National Ambient Air  
Quality Standards: Second Draft

appearing on behalf of the  
American Petroleum Institute

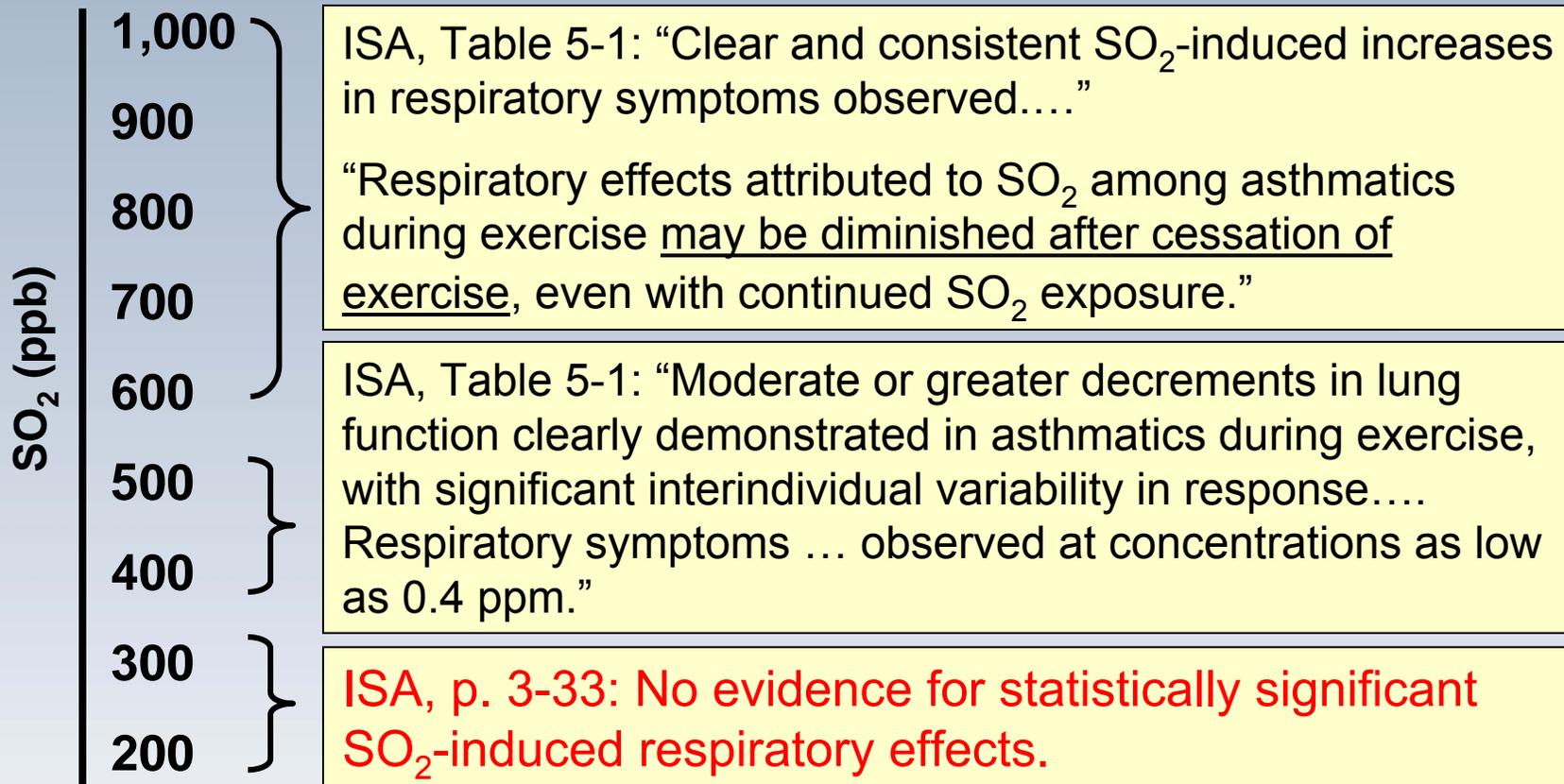
April 16, 2009

# There is No Basis for the Suggested 1-hr Daily Max SO<sub>2</sub> NAAQS

- Human clinical studies of exercising mild-to-moderate asthmatics show no statistically significant increase of respiratory symptoms at SO<sub>2</sub> peak exposures < 400 ppb.
- Epidemiological studies do not support the suggested 1-hr daily max SO<sub>2</sub> NAAQS.



# Health Effects of Short-Term Exposure to SO<sub>2</sub> in Clinical Studies\*



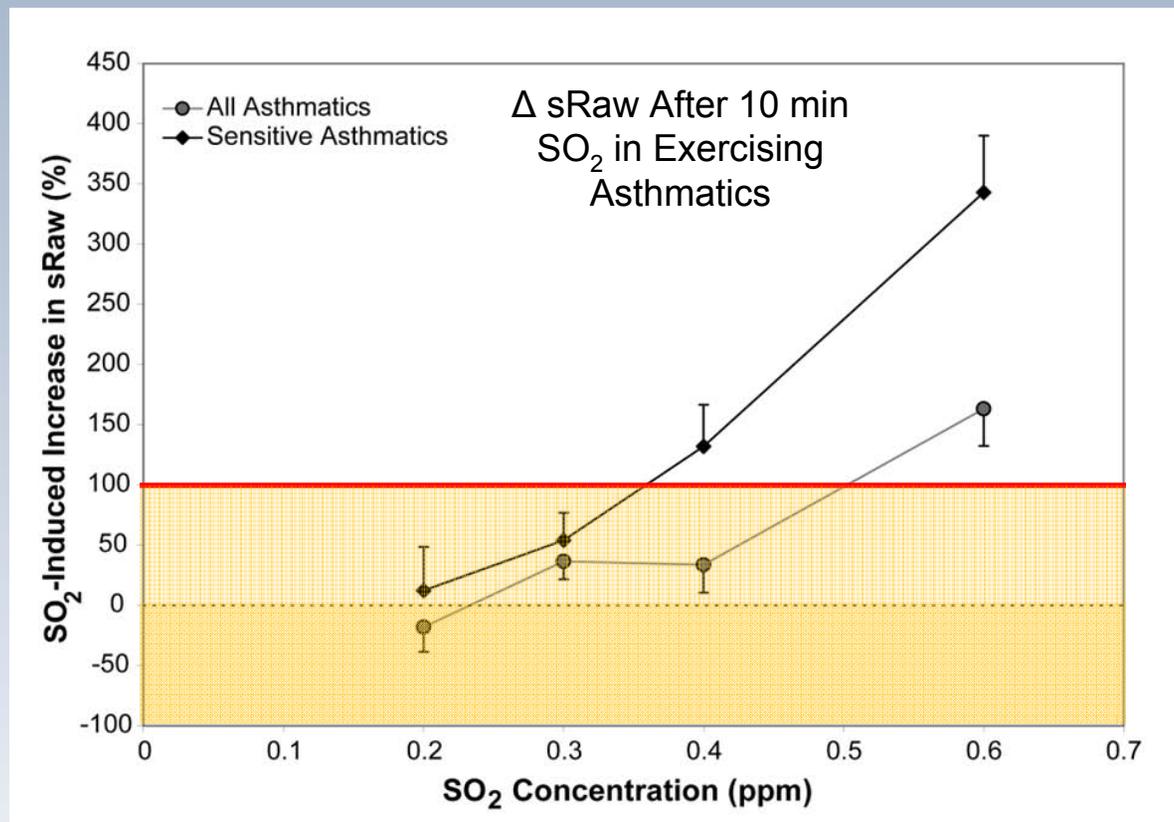
\*Subjects are asthmatics during exercise

# Interpretation of Effects in Clinical Studies

- NAAQS should protect against *adverse* effects.
- A transient decrement in lung function should not automatically be considered an adverse effect.
- 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.



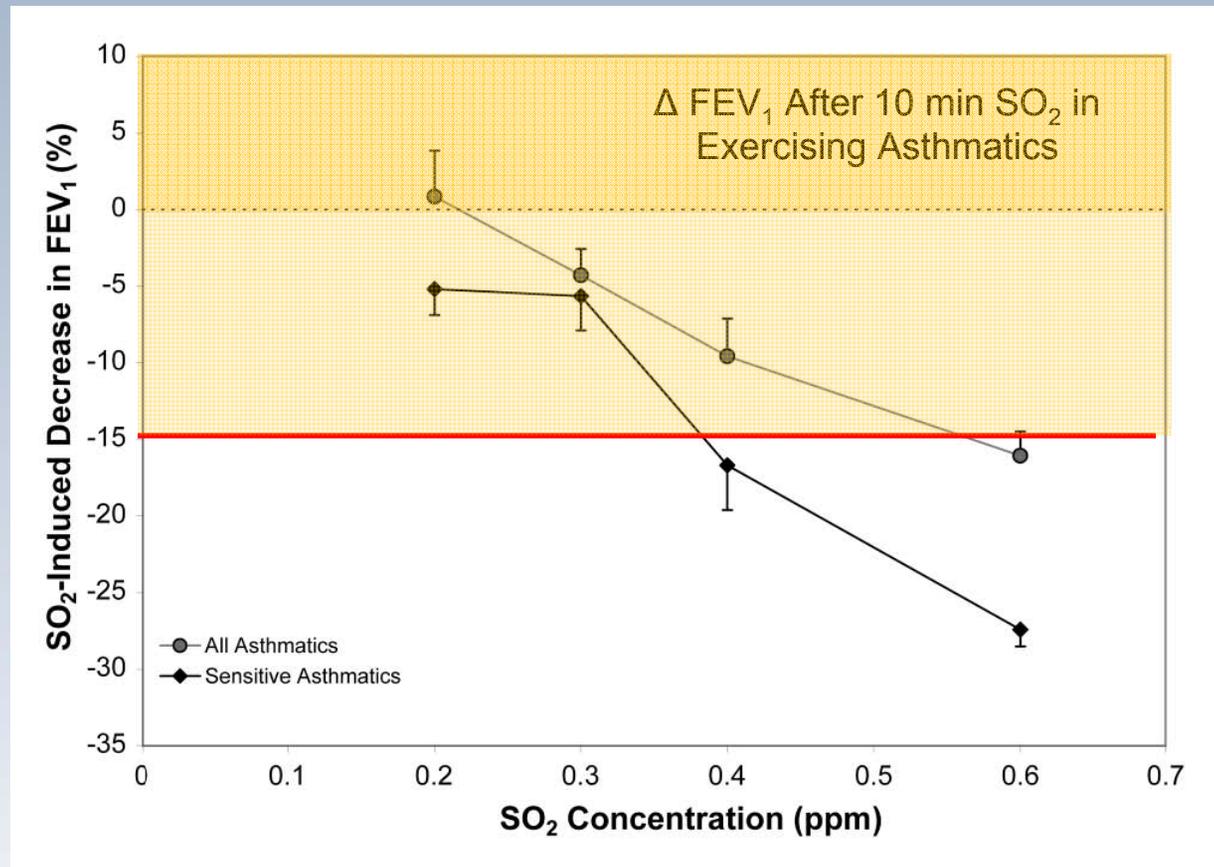
REA defines a “moderate or greater lung function decrement” as  $\geq 100\%$  increase in sRaw or  $\geq 15\%$  decrease in FEV<sub>1</sub>.



Final ISA Figure 4-2



REA defines a “moderate or greater lung function decrement” as  $\geq 100\%$  increase in sRaw or  $\geq 15\%$  decrease in FEV<sub>1</sub>.



Final ISA Figure 4-3



# Lower Benchmarks for Short-term SO<sub>2</sub> Suggested in REA are NOT Appropriate

- Effects observed below 400 ppb SO<sub>2</sub> CANNOT be considered adverse by the REA definition ( $\geq 100\%$  increase in sRaw or  $\geq 15\%$  decrease in FEV<sub>1</sub>).
- No effects observed below 400 ppb SO<sub>2</sub> are statistically significant.
- The lowest exposures at which *statistically significant adverse* effects occur are  $\geq 400$  ppb.
- It is highly unlikely that asthmatics would experience *adverse* effects, according to the REA definition, at exposures  $\leq 200$  ppb.



# Clinical Studies Account for Sensitive Individuals

- Clinical subjects included adolescent and adult asthmatics at exercise.
- Asthmatic adolescents exposed *via* mouthpiece (results in higher SO<sub>2</sub> exposure than real world).
- Linn *et al.* (1987) found responses of moderate/severe asthmatics to increasing SO<sub>2</sub> concentrations were roughly similar to those of minimal/mild asthmatics.
- Responses to SO<sub>2</sub> not strongly dependent on clinical severity of asthma.



# Clinical Studies Assess Rare Event in Sensitive Individuals

- Clinical studies do not represent real world scenarios.
- Unmedicated asthmatics engaged in moderate exercise is not a common event.
- Exercise does not generally occur near an SO<sub>2</sub> source that has the potential to produce high ground level SO<sub>2</sub> concentrations.
- If peak short-term SO<sub>2</sub> exposure of 600-1,000 ppb, respiratory effects typically diminish with cessation of exercise, **EVEN IF** high SO<sub>2</sub> exposures continue.



# No Epi Support for 1-hr Daily Max SO<sub>2</sub> NAAQS

- Majority of studies reported null or weakly positive findings
- Weakly positive findings often became non-significant when adjusted for co-pollutants
- Information on co-pollutants or other exposure-related factors was not included in many studies
- Exposure misclassification could have biased results in either direction
- Measurements from central monitors are not representative of human exposure
  - Spatial and temporal variability
  - Association between ambient concentrations and personal exposures are inadequately characterized.
- Findings inconsistent with better-controlled human clinical studies

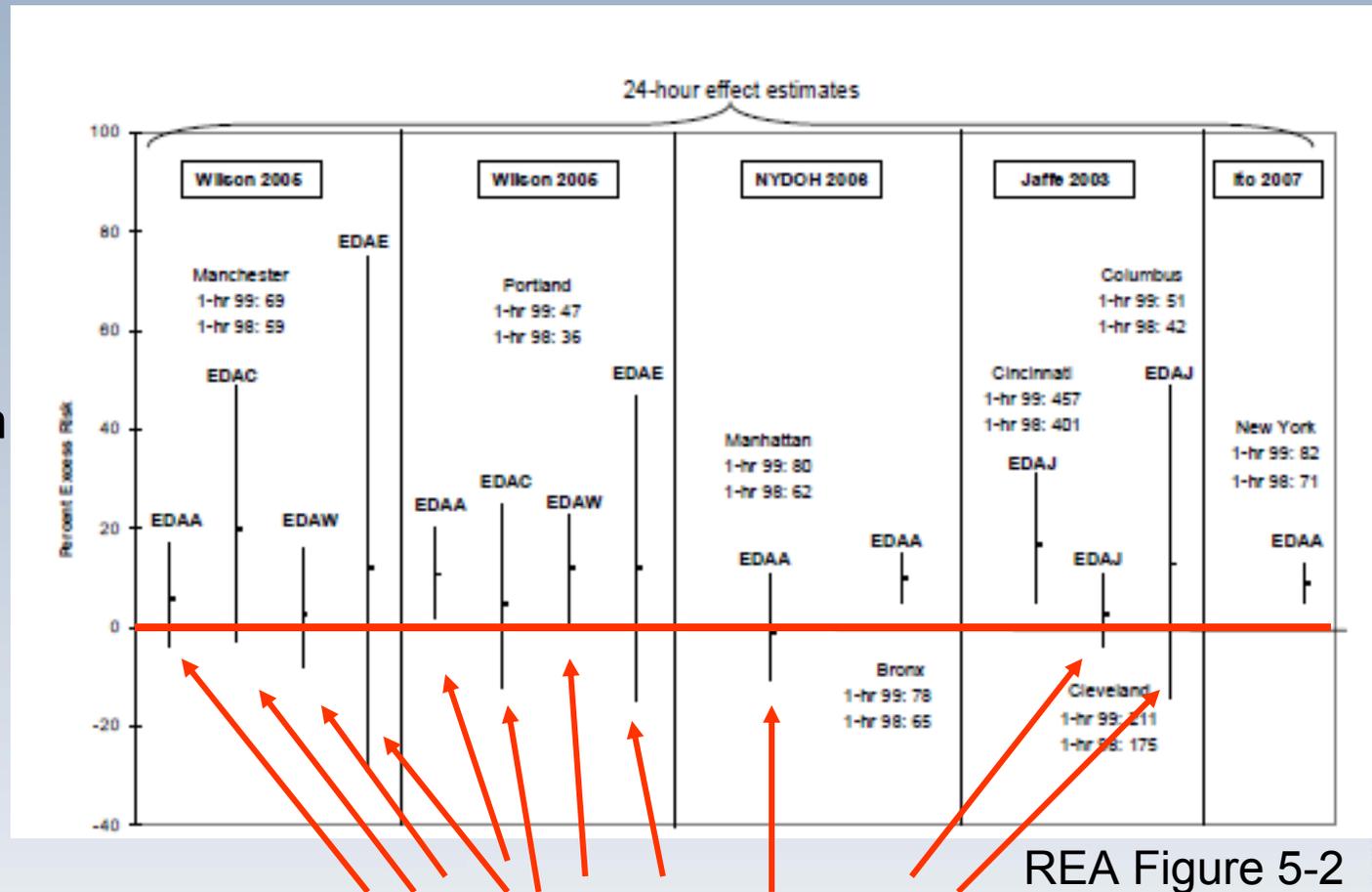


# Risk Estimates are Very Small

- Many not statistically significant

## Additional Bias

- Exposure misclassification
- Known confounders
- Residual confounding
- Unmeasured confounders
- Unknown confounders



Not statistically significant

REA Figure 5-2

# Conclusions

- Clinical data do not support the suggested 1-hr daily max SO<sub>2</sub> NAAQS
  - Includes sensitive individuals (asthmatics, adolescents)
  - Exposure scenario is rare event
  - If symptoms do occur, relief by discontinuing exercise
  - Effects at exposures < 400 ppb do NOT meet REA's definition of adverse
  - Effects at exposures < 400 ppb are NOT statistically significant
  - Use of clinical data incorporates “safety factors”
- Epidemiology studies do not support the suggested 1-hr daily max SO<sub>2</sub>

