

Sagai and Ichinose, 1991

Guidelines/Criteria	
	Reference: Sagai M, Ichinose T. 1991. Biochemical effects of combined gases of nitrogen dioxide and ozone. IV. Changes of lipid peroxidation and antioxidative protective systems in rat lungs upon life span exposure. Toxicology 66:121-132.
In vivo Study Type Route of Administration Species & age of animals	Chronic inhalation study Inhalation Male Wistar rats
Study Duration	22 months
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes No Unknown Lung toxicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Lung homogenate thiobarbituric acid (TBA) reactant (indicator of lipid peroxidation) and various other measures which were no more sensitive and more biochemical/pharmacological Unknown
Individual Components Characterisation of individual compounds Name, exact chemical name, CAS no. Were dose responses established for individual components? Were no effect levels established? Were doses below the NO(A)ELs investigated?	Nitrogen dioxide and ozone No, only single doses were tested for ozone, though three were tested for nitrogen dioxide (in a related paper by the same authors) Yes, 0.05 ppm for ozone (only dose tested) and 0.04 ppm for nitrogen dioxide (lowest dose tested). The next dose of NO ₂ , 0.4ppm, had no effect at the 9 month timepoint, but the related paper shows it had a clear effect at 18 months and so it cannot be considered to be a NOEL. No
Mixtures Investigated Number of dose levels How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?) No. of technical replicates per exposure condition (<i>in vitro</i>) No. of animals per dose group (<i>in vivo</i>)	1 only that is relevant, i.e. at a NOEL of each component. No particular rationale.
Observations/Findings	At the one relevant mixture concentration (1x NOEL of both components), there was an increase in TBA reactants.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Good paper, but only one relevant dose level.