

Guidelines/Criteria	
	Reference: Cometto-Muñiz JE, Cain WS, Abraham MH, Gola JMR. 2001. Ocular and nasal trigeminal detection of butyl acetate and toluene presented singly and in mixtures. Toxicol Sci 63(2):233-244.
In vivo Study Type Route of Administration Species & age of animals	Airborne Human, various ages, osmic and anosmic
Study Duration	Series of single tests
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes None Not defined; one ester and one cyclic aromatic tested Trigeminal nerve stimulation (nasal pungency, eye irritation)
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Nose (pungency), eye (irritation) Pharmacological (odour), adverse (nasal pungency and eye irritation)
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?	Butyl acetate (99+%), toluene (99.8%) Yes Yes, stimulus-response (psychometric) functions were established using two-fold (for butyl acetate) and 1.5-fold (for toluene) dilution steps. Yes, in terms of varying probabilities of detection by individual subjects
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 No. of subjects per dose group (<i>in vivo</i>)	3 detection probability levels for eye irritation; 4 for nasal pungency. Each level consisted of 5 tests (2 for the single substances, 3 mixtures) Probabilities (p) of detection for specific concentrations were calculated: for eye irritation 0.50, 0.75, and 1.00, for nasal pungency also 0.25. Binary mixtures included p of 0.25, 0.50 and 0.75 of one chemical combined with each level of the other (i.e. 3 mixtures). Each subject participated in 4 to 8 sessions of varying length and replicates. Twelve normosmic subjects, age 19 - 51 y Six anosmic subjects, 34 - 74 y For eye irritation of binary mixtures, only normosmic subjects participated; for nasal pungency, only anosmic subjects were entered.
Observations/Findings	For both endpoints similar findings were seen: at relatively low levels of detection for single compounds (< 0.50) complete agonism was seen for the mixtures. At higher levels (p of detection > 0.50) the mixtures showed partial agonism.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	The same strengths and weaknesses as for Cometto-Muñiz 1999 apply: reasonable number of subjects and replicates, use of detectability (psychometric functions, but only binary mixtures were tested.