

Stacey, 1989

Guidelines/Criteria	
Reference:	Stacey NH. 1989. Toxicity of mixtures of trichloroethylene, tetrachloroethylene and 1,1,1-trichloroethane: similarity of in vitro to in vivo responses. Toxicol Ind Health5(3):441-450.
<b>In vivo Study Type</b> Route of Administration Species & age of animals	See also <i>in vitro</i> tab for another study in the same paper i.p. male Sprague-Dawley rats
<b>Study Duration</b>	24 h (single dose administration)
<b>Type of Mixture</b> Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	yes yes similar action assumed Hepatotoxicity
<b>Parameters/End points Measured</b> Target organs/Critical effects Pharmacological changes or adverse effects	Hepatotoxicity (ALT, SDH sorbitol dehydrogenase, Urea) enzyme changes
<b>Individual Components</b> 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?	yes Trichloroethylene, Tetrachloroethylene, 1,1,1-trichloroethane No Yes No
<b>Mixtures Investigated</b> 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> )	Chemicals were administered alone in two-way and three-way combinations: Trichloroethylene 10 mmol/kg bw Tetrachloroethylene 15 mmol/kg bw 1,1,1-Trichloroethane 15 mmol/kg bw or combinations of these doses administered doses were close to thresholds  not applicable 5 or 6 animals / dose group
<b>Observations/Findings</b>	No response in ALT, SDH, urea for the individual chemicals. Each binary and the tertiary mixtures showed increased ALT, SDH and urea levels.
<b>Overall opinion</b> (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Limited relevance; limited parameters assessed.

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<b>In vitro Study Type</b> Route of Administration Species & age of animals	Primary rat hepatocytes
<b>Study Duration</b>	3 h
<b>Type of Mixture</b> Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes Yes Similar Simply cytotoxicity
<b>Parameters/End points Measured</b> Target organs/Critical effects Pharmacological changes or adverse effects <i>In vitro</i>	Loss of intracellular potassium, ALT and LDH
<b>Individual Components</b> 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?	Trichloroethylene, Tetrachloroethylene, 1,1,1-trichloroethane Yes, in a preliminary study  Yes, and doses used were below threshold for cytotoxicity. Exact doses used are not meaningful as the cultures were exposed via the vapour phase. No
<b>Mixtures Investigated</b> 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> )	A sub-threshold dose for each chemical was used (High), and a lower dose (approximately half - Low) Same two doses was used for each chemical whether dosed singly or in mixtures. All combinations were tested, ie 12 two component mixtures and 8 three component combinations  Experiments were repeated four to five times
<b>Observations/Findings</b>	Similar effects were seen with all three endpoints. For the two and three component mixtures, none containing only Low doses produced effects, whilst almost all containing at least one High dose did produce an effect.
<b>Overall opinion</b> (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Overall the study appears well conducted. Defining absolute doses is always a problem for volatiles <i>in vitro</i> .