Stacey, 1987

Guidelines/Criteria	
Reference:	Stacey NH. 1987. Assessment of the toxicity of chemical mixtures with isolated rat hepatocytes: Cadmium and chloroform. Fundam Appl Toxicol 9:616-622.
***In vitro* Study Type** Route of Administration Species & age of animals	Primary rat hepatocytes
Study Duration	1 h and 3 h
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Yes No Superficially similar - both hepatotoxic Simply cytotoxicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects *In vitro*	 Loss of intracellular potassium and aspartate aminotransferase and lactate/pyruvate ratio (intracellular potassium was the most sensitive)
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?	 Cadmium chloride and chloroform Yes, in the present study Yes, 25 uM for Cd and 30 mM for chloroform in the case of the potassium endpoint (AST and lactate/pyruvate endpoints were less sensitive) Yes for chloroform (15 mM)
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 (*in vitro*) No. of animals per dose group (*in vivo*)	 All combinations of Cd at 25, 50 & 100 uM and chloroform at 15, 30 & 60 mM Includes effect and no-effect levels for both components Experiments were repeated four to seven times
Observations/Findings	Effects on intracellular potassium seen at the combination of NOELs (25 uM Cd & 30 mM chloroform) and at a lower concentration of chloroform (25 uM Cd & 15 uM chloroform). Speculates that this relates to glutathione depletion by chloroform.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	 Overall the study appears well conducted and comprehensive. However, lower dose combinations were not used and there was no mixture that produced no effect.