

Guidelines/Criteria	
	Reference: Narotsky MG, Weller EA, Chinchilli VM, Kavlock RJ. 1995. Nonadditive developmental toxicity in mixtures of trichloroethylene, di(2-ethylhexyl) phthalate, and heptachlor in a 5 x 5 x 5 design. Fundam Appl Toxicol 27:203-216.
In vivo Study Type Route of Administration Species & age of animals	oral, gavage Fischer -344, 90-day old females, Day 6-15 gestation
Study Duration	Day 6 gestation until day 6 postpartum
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	no 3 response additivity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	pups developmental effects
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?	Trichloroethylene (TCE) di(2-ethylhexyl) phthalate (DEHP) heptachlor (HEPT) corn oil (vehicle) yes For HEPT and DEHP For mixture experiment not clear For TCE and DEHP For mixture unclear from article
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>)	5 Linear regression from single substances doses creating 2 g weight loss on GD 6-8 10-12
Observations/Findings	Synergistic developmental tox for several endpoints. The DEHP-HEPT, were synergistic for maternal mortality. HEPT potentiated the effect of tCE and DEHP for Full litter resorption and prenatal loss. Beside response additivity also examples of dose-additivity were found.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Very complex study design, adequate group sizes, only partly reproducible. No real low doses tested.