

Guidelines/Criteria	
	Reference: Donnelly KC, Claxton LD, Huebner HJ, Capizzi JL. 1998. Mutagenic interactions of model chemical mixtures. Chemosphere 37(7):1253-1261.
In vitro Study Type	Ames test
Study Duration	72 hours
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	All binary combinations of three compounds Combination of three compounds Similar Mutagenicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects In vitro	Revertant colonies in 3 Salmonella strains +/- S9
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?	Benzo(a)pyrene (BaP), pentachlorophenol (PCP), 2,4,6-trinitrotoluene (TNT) Yes Yes, shown on right (all units are ug/plate) Yes for all mixtures in some strains
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)	5 levels with a fixed ratio of components Complex - this is effectively a full mixture study on 6 strains (3 strains +/-S9) 4
Observations/Findings	Overall, if all chemicals were present at a NOEL then the mixture produced no effect (70 instances, with 1 exception where an effect was seen). When at least one chemical was present at an effect level was usually seen (44 instances, with 5 exceptions where no effect was seen).  When the fractions of the individual component NOELs were added up, then the mixture NOELs were .6x to 10x the NOEL, and the mixture LOELs were to 1.4x to 25x the NOEL.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Good study. There were 1-5 doses below the NOEL of all components, depending on the strain and mixture considered. A robust test of all 2 and 3-way mixtures, showing a tendency for less than additive effects overall.

		TA97a -S9	TA97a +S9	TA98 -S9	TA98 +S9	TA100 -S9	TA100 +S9
NOEL	BaP	200	50	200	50	200	50
NOEL	PCP	200	200	200	200	200	200
NOEL	TNT	40	2400	400	4800	400	1000
Mixture NOEL total as multiple of the sum of the individual component NOEL	BaP+PCP	2	1.25	2	1.25	2	1.25
	BaP+TNT	1.01	0.57	2.75	5	1.1	2
	PCP+TNT	1.01	1.5	2.75	2	1.1	1.25
	BaP+PCP+TNT	10.2	1.67	3	3	1.2	2.25
Mixture LOEL total as multiple of the sum of the individual component NOEL	BaP+PCP		2.5		2.5		2.5
	BaP+TNT	10.1	1.42	6.5		2.75	4.4
		10.1	3	6.5		2.75	2.9
	PCP+TNT						
	BaP+PCP+TNT	25.5	3.5	7	6	2.75	4.9