

Guidelines/Criteria	
	Reference: Rajapakse N, Silva E, Kortenkamp A. 2002. Combining xenoestrogens at levels below individual no-observed-effect concentrations dramatically enhances steroid hormone action. Environ Health Perspect 110(9):917-921.
In vitro Study Type Route of Administration Species & age of animals	Yes
Study Duration	72 h treatment
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	no 12 component mixture; three fixed mixture ratios similarly acting CA and effect summation
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects <i>In vitro</i>	hER activation via beta-galactosidase expression
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?	estradiol; 2,3,4,5-tetrachlorobiphenyl-4-ol; 2,5-dichlorobiphenyl-4-ol; 4-chlorobiphenyl-4-ol; genistein; 2,4-dihydroxybenzophenone; benzyl-4-hydroxyparabene; 2,3,4,5-tetrachlorobiphenyl; BPA; resorcinol monobenzoate; 2,3,4-trichlorobiphenyl; phenyl salicylate. No CAS numbers in paper yes NOECs and EC01s yes/no - due to fact that well characterised dose-responses, NOECs very close to EC01s.
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>)	10 per mixture; 3 mixture ratios ratio of XEs based on EC01s then mixed with E2 at 1:100000 to 1:25000. Run at least twice in triplicates
Observations/Findings	Modulation of E2 by combination of XEs where each present well below Effect levels. Predicted by Concentration Addition.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Relevant for this Task Force's review, though not aiming to replicate real-life levels.