

Guidelines/Criteria	
	Reference: Gaido KW, McDonnell DP, Korach KS, Safe SH. 1997. Estrogenic activity of chemical mixtures: Is there synergism? <i>CIIT Activities</i> 17(2):1-7.
In vitro Study Type	Yeast-based human oestrogen receptor gene transcription assay
Study Duration	24hrs
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes No Depends on your perspective Oestrogen receptor activity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects <i>In vitro</i>	Beta-galactosidase activity (indicating gene transcription)
Individual Components Characterisation of individual compounds Name, exact chemical name, CAS no. Were dose responses established for individual components? Were no effect levels established?	Endosulfan, chlordane, toxaphene and dieldrin Yes There were two types of experimental conditions, one with a high level of oestrogen receptor expression and one with a low level. For high oestrogen receptor expression the NOEL was 10e-5 M for endosulfan, and for chlordane, toxaphene and dieldrin there was no effect at the top dose, which was 10e-4 M. For the low level of oestrogen receptor expression no chemical caused an effect at the same top dose.
Were doses below the NO(A)ELs investigated?	Yes
Mixtures Investigated Number of dose levels How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?)	All 6 pairwise mixtures were tested at three concentrations Equimolar concentrations were used. At high oestrogen receptor expression level, the mixtures contained 0.05x & 0.5x the NOEL of endosulfan, and/or 0.005x, 0.05x & 0.5x the NOEL of the other single components. At low oestrogen receptor expression level, the mixtures contained 0.005x, 0.05x & 0.5x the NOEL of all single components
No. of technical replicates per exposure condition (<i>in vitro</i>)	Not stated
Observations/Findings	No effects seen for any treatments where each component was at a NOEL
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Seems well conducted. An attempt to replicate the conditions used by Arnold et al. The same paper reports a combination of two PCBs in a HepG2 oestrogen receptor assay, but no stats are presented so NOELs cannot be determined. The same paper reports an MCF-7 assay with toxaphene and dieldrin, but the mixture was not tested at a NOEL of both components. The same paper reports a competitive binding assay in MCF-7 cells with toxaphene and dieldrin, but this is not a toxic endpoint and thus, paper not relevant for this report. There is also an <i>in vivo</i> assay in this paper - see other tab.

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	Reference: Gaido KW, McDonnell DP, Korach KS, Safe SH. 1997. Estrogenic activity of chemical mixtures: Is there synergism? CIIT Activities 17(2):1-7.
In vivo Study Type Route of Administration Species & age of animals	Uterotrophic assay Immature female mice
Study Duration	3 or 4 days
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes No Potentially similar Oestrogenicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Uterine weight Debatable
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?	Toxaphene, dieldrin No Yes, there was no effect at the single dose tested, 60 umol/kg/day. No
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>)	Equimolar, 30 umol/kg/day of each 6 to 9
Observations/Findings	No effect of the mixture, which was at 0.5x NOEL of both components
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Some details are missing in the reporting. Progesterone receptor concentration and peroxidase activity in the uteri were also measured, with the same result as uterine weight.