Soto et al, 1994

Guidelines/Criteria	
Reference:	Soto AM, Chung KL, Sonnenschein C. 1994. The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells. Environ Health Perspect 102(4):380-383.
***In vitro* Study Type** Route of Administration Species & age of animals	Human oestrogen-sensitive breast cancer MCF7 cells (E-screen test)
Study Duration	6 days
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Mixture of 10 pesticides/metabolites Assumed to have oestrogenic activity Neutralisation of the inhibitory effect of a human serum-borne molecule on proliferation of human oestrogen-sensitive cells
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects *In vitro*	 Proliferative activity compared to hormoneless control
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?	 endosulfan beta, endosulfan alpha, toxaphene, dieldrin, 2,3,4,5-tetrachlorobiphenyl, p,p'-DDT, 2,2',3,3',6,6'-hexachlorobiphenyl, p,p'-DDD, p,p'-DDE, methoxychlor Yes, compounds were tested at 5 concentrations ranging from 1 nM to 10 uM Yes - 1 uM for all chemicals Yes
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*)	 One All individual components were applied at 1 uM, i.e. at the NOEC Duplicate wells repeated at least 5 times
Observations/Findings	The individual compounds only showed a significant effect at concentrations 6 orders of magnitude higher than the reference compound estradiol. The combination of 10 compounds tested at 1 uM showed a weak additive effect (less than the proliferative effect seen with the single compound endosulfan beta at 10 uM).
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	There has to be a question mark over the test results of the individual compounds - the fact that they should all show the same effect at the same concentration is somewhat surprising. Testing of the 10-compound mixture was done at individual NOECs and showed a weak additive response. Lower concentrations were not tested in mixture. This study is therefore of limited relevance for the Task Force's review.