Guidelines/Criteria		
Reference:	Wade MG, Desaulniers D, Leingartner K, Foster WG. 1997. Interactions between endosulfan and dieldrin on estrogen-mediated processes in vitro and in vivo. Reprod Toxicol 11(6):791-798.	
***In vitro* Study Type** Route of Administration Species & age of animals	Rat uterine oestrogen receptor binding	MCF-7 cell proliferation assay
Study Duration	1hr	unclear
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Yes No Perhaps similar Oestrogenicity	 Yes No Perhaps similar Oestrogenicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects *In vitro*	 Displacement of tritiated oestrogen	 Proliferation of MCF-7 cells
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 and dieldrin Yes Yes. At a high concentration of receptors the NOEL of dieldrin was 10E-5 M and of endosulfan was 2x10E-6 M. At a low concentration of receptors the NOEL of dieldrin and endosulfan were both 4x10E-7 M. Yes	 Endosulfan and dieldrin Yes Yes. On basal medium NOEL was 10 um for dieldrin and 2 uM for endosulfan. On medium with a subthreshold concentration of oestrodiol there was no NOEL established for either, so these data re not relevant for us. 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*)	 4 relevant mixtures at high receptor concentration and 3 at a low receptor concentration. Equimolar. At the high receptor concentration the mixtures contained 0.0008x NOEL + 0.004x NOEL, 0.004x NOEL + 0.02x NOEL, 0.02x NOEL + 0.1x NOEL, and 0.1x NOEL + 0.5x NOEL of dieldrin and endosulfan respectively. At the low receptor concentration the mixtures contained 0.02x NOEL, 0.1x NOEL and 0.5x NOEL of both components. Three duplicate determinations	 2 relevant mixtures (on basal medium) Equimolar. The relevant mixtures contained 0.02x NOEL for dieldrin + 0.1x NOEL for endosulfan, and 0.1x NOEL for dieldrin + 0.5x NOEL for endosulfan. Three experiments each with 4 replicate incubations
Observations/Findings	No effect seen at an mixture concentrations where each component was at a NOEL.	No effect seen at an mixture concentrations 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)	Good study. There was also an *in vivo* study in the same paper - see other tab.	Good study.

Wade et al, 1997

Guidelines/Criteria	
Reference:	Wade MG, Desaulniers D, Leingartner K, Foster WG. 1997. Interactions between endosulfan and dieldrin on estrogen-mediated processes in vitro and in vivo. Reprod Toxicol 11(6):791-798.
In vivo **Study Type** Route of Administration Species & age of animals	Rat uterotrophic assay ip Female Sprague-Dawley rats
Study Duration	Dosed for 3 days from day 18 of life and terminated at day 21
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Yes No Potentially similar Oestrogen receptor activation
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	 Uterine weight (progesterone receptors, uterine peroxidase activity, oestrogen receptors and various hormone concentrations were also quantified) 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?	 Endosulfan and dieldrin No, only single doses were tested (3mg/kg/d) No effects seen at the single dose tested 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 (*in vitro*) No. of animals per dose group (*in vivo*)	 1 only No particular rationale. The mixture tested was at the single dose which had been tested for each component separately. 10
Observations/Findings	No effect on uterine weight or any other endpoint for either chemical alone or in combination.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	 Good study, but only one dose level and of limited value to the Task Force's review.