

Guidelines/Criteria	
Reference:	Heindel JJ, Chapin RE, Gulati DK, George JD, Price CJ, Marr MC, Myers CB, Barnes LH, Fail PA, Grizzle TB, Schwetz BA, Yang RSH. 1994. Assessment of the reproductive and developmental toxicity of pesticide/fertilizer mixtures based on confirmed pesticide contamination in California and Iowa groundwater. <i>Fundam Appl Toxicol</i> 22:605-621.
<b>In vivo Study Type</b> Route of Administration Species & age of animals	drinking water, water control and vehicle control group Swiss CD-1 mice (11 week of age)
<b>Study Duration</b>	Reproductive assessment by continuous breeding (7 days pre mating, 98 days breeding in breeding pairs, pairs are separated, selected F1 pups are reared in same sex groups for 74 days +/- 10 days of age, cohabitation for 7 days, housed singly until delivery of F2 generation
<b>Type of Mixture</b> Binary >2 components  Similar acting or dissimilar  What Mode of Action was investigated?	no yes (propylene glycol was added as a vehicle to each mixture to solubilize the pesticides in drinking water) dissimilar action assumed (pesticide/fertilizer mixtures representing up to 100-fold ground water contamination reproduction toxicity (no specific mode of action)
<b>Parameters/End points Measured</b> Target organs/Critical effects   Pharmacological changes or adverse effects	Clinical signs, parental body weight, fertility (number producing a litter/number of breeding pairs), litters per pair, live pups per litter, proportion of pups born alive, sex of live pups, pup body weights within 24 hr after birth, feed and water consumption, organ weight determination and histopathology of selected F1 organs, spermatology adverse effects
<b>Individual Components</b> 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?	yes Two mixtures were investigated: 1. Alachlor (15972-60-8), Atrazine (1912-24-9), Cyanazine (21725-46-2), Metolachlor (51218-45-2), Metribuzine (21087-64-9), Ammonium nitrate (6484-52-2), Propylene glycol (57-55-6) 2. Aldicarb (116-06-3), Atrazine (1912-24-9), Dibromochloropropane (96-12-8), 1,2-Dichloropropane (78-87-5), Ethylenedibromide (106-93-4), Simazine (122-34-9), Ammonium nitrate (6484-52-2), Propylene glycol (57-55-6) No, only mixtures at three dose levels were administered Yes: No effects were seen at each dose level Yes
<b>Mixtures Investigated</b> 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> )	Each 3 dose groups containing the individual compounds at the following doses (representing 1x, 10x, 100x of observed ground water contamination): Mixture 1 Alachlor: 0.17 - 17.2 µg/kg bw, Atrazine: 0.09 - 9.5 µg/kg bw, Cyanazine: 0.07 - 7.6 µg/kg bw, Metolachlor: 0.07 - 7.6 µg/kg bw, Metribuzine: 0.12 - 12.4 µg/kg bw, Ammonium nitrate: 1.7 - 177.5 µg/kg bw Mixture 2: Aldicarb: 1.8 - 184.2 µg/kg bw, Atrazine: 0.1 - 10.2 µg/kg bw, Dibromochloropropane: 0.002 - 0.2 µg/kg bw, 1,2-Dichloropropane: 0.90 - 92 µg/kg bw, Ethylenedibromide: 0.182 - 18.2 µg/kg bw, Simazine: 0.061 - 6.1 µg/kg bw, Ammonium nitrate: 2.0 - 204.8 µg/kg bw Each dose group corresponded most likely to a low dose;  not applicable 20 pairs/group (40 control pairs)
<b>Observations/Findings</b>	At 100x of the second mixture: decreased seminal vesicle weights, decreased average days to litter, increased kidney/adrenal weights in female F1 mice; increased ovary weights seem to be within historical control data; otherwise no effects observed
<b>Overall opinion</b> (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Good study design, sufficient number of animals, relevant endpoints; Developmental NOELs of the individual compounds are partly given in the report; Low dose levels investigated