

# NTP Report 36 mice

<b>Guidelines/Criteria</b>	
Reference:	NTP. 1993b. NTP Technical Report on toxicity studies of pesticide/fertilizer mixtures administered in drinking water to F344/N rats and B6C3F1 mice. NTP Toxicity Report series no. 36 - NIH Publication 93-3385. National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC, USA.
<b>In vivo Study Type</b> Route of Administration Species & age of animals	drinking water; water control and vehicle control group CD-1 Swiss mice, 40-41 days old
<b>Study Duration</b>	26-weeks study
<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	body weight, food and water intake, organ weights (heart, right kidney, liver, lungs, right testis, thymus), macroscopic and histopathological examinations, clinical chemistry and haematology (days 92, 183), urinalysis (days 3, 18, 88, 179), vaginal cytology and sperm morphology (13-week interim), neurobehavioural and neuropathologic evaluations (home cage and open field, motor activity, forelimb, hind limb strength), frequency of micronuclei in splenocytes and in peripheral blood of female mice induction of sister chromatid exchanges in splenocytes of female mice (only for 1x, 10x, 100x mixture) 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 no
<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 4 dose groups containing the individual compounds at the following doses (representing 0.1x, 1x, 10x, 100x of observed ground water contamination):: Mixture 1 (Iowa mixture) Alachlor: 0.09, 0.9, 9, 90 ppb, Atrazine: 0.05, 0.5, 5, 50 ppb, Cyanazine: 0.04, 0.4, 4, 40 ppb, Metolachlor: 0.04, 0.4, 4, 40 ppb, Metribuzine: 0.06, 0.6, 6, 60 ppb, Ammonium nitrate: 1, 10, 100, 1000 ppb Mixture 2 (California mixture): Aldicarb: 0.3, 3, 30, 300 ppb, Aldicarb sulfone: 0.3, 3, 30, 300 ppb, Aldicarb sulfoxide: 0.3, 3, 30, 300 ppb, Atrazine: 0.05, 0.5, 5, 50 ppb, Dibromochloropropane: 0.001, 0.01, 0.1, 1 ppb, 1,2-Dichloropropane: 0.45, 4.5, 45, 450 ppb, Ethylenedibromide: 0.09, 0.9, 9, 90 ppb, Simazine: 0.03, 0.3, 3, 30 ppb, Ammonium nitrate: 1, 10, 100, 1000 ppb The 1x concentrations represents human exposure levels  not applicable 20 male and female animals/group + additional satellite groups
<b>Observations/Findings</b>	Slightly decreased body weight change in the top dose males at the 13 week and the interim and the terminal sacrifice. Decreased absolute and relative liver weights in male mice of the 100x dose group of the California mixture. Induction of micronuclei in peripheral blood: Increased incidences are observed in the Iowa mixture starting from 10x without a clear dose-response relationship (1.54 +/- 0.12, 2.39 +/- 0.49, 3.33 +/- 0.22, 2.72 +/- 0.42). Increased incidences of sister chromatid exchange in splenocytes at 100 x in the Iowa mixture.
<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; good documentation. Low dose levels investigated.