NTP Report 35 Chapin et al, 1989

Guidelines/Criteria	
Reference:	NTP. 1993a. NTP Technical Report on toxicity studies of a chemical mixture of 25 groundwater contaminants. NTP toxicity report series no. 35 - NIH Publication 93-3384. National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC, USA Chapin RE, Phelps JL, Schwetz BA, Yang RSH. 1989. Toxicology studies of a chemical mixture of 25 groundwater contaminants. III. Male reproduction study in B6C3F1 Mice. Fundam Appl Toxicol 13:388-398.
***In vivo* Study Type**	
Route of Administration	drinking water, water control group
Species & age of animals	B6C3F1 mice, 8 weeks
Study Duration	90 days
Type of Mixture	
Binary	no
>2 components	yes
Similar acting or dissimilar	dissimilar action assumed (chemicals mix to simulate groundwater supplies near hazardous dumps)
What Mode of Action was investigated?	repeated dose toxicity
Parameters/End points Measured	
Target organs/Critical effects	Male reproduction spermatogenesis, liver, kidney, testis, epididymis, seminal vesicles
Pharmacological changes or adverse effects	adverse effects
Individual Components	
Characterisation of individual compounds	yes
Name, exact chemical name, CAS no.	One mixture was investigated: Acetone, Aroclor 1260, Arsenic, Benzene, Cadmium, Carbon tetrachloride, Chloroform, Chlorobenzene, Chromium, 1,1-Dichloroethane, 1,1-Dichloroethylene, 1,2-Dichloroethane, 1,2-t-Dichloroethylene, Di/2-ethylhexyl)phthalate, Ethylbenzene, Lead, Mercury, Methylene chloride, Nickel acetate tetrahydrate, Phenol, Tetrachloroethylene, Toluene, 1,1,1-Trichloroethane, Trichloroethylen, Xylenes
Were dose responses established for individual components?	No, only mixtures at three dose levels were administered: Target dose (see below and 2 and 10 fold dilutions thereof)
Were no effect levels established?	Yes
Were doses below the NO(A)ELs investigated?	Yes presumably
Mixtures Investigated	
Number of dose levels	Target concentrations: Acetone: 53 ppm, Aroclor 1260: 0.01 ppm, Arsenic: 9.0 ppm, Benzene: 12.5 ppm, Cadmium: 51.0 ppm, Carbon tetrachloride: 0.40 ppm, Chloroform: 7.0 ppm, Chlorobenzene: 0.10 ppm, Chromium: 36.0 ppm 1,1-Dichloroethane: 1.4 ppm, 1,1-Dichloroethylene: 0.5 ppm, 1,2-Dichloroethane: 40.0 ppm, 1,2-t-Dichloroethylene: 2.5 ppm, Di-2-ethylhexyl)-phthalate: 0.015 ppm, Ethylbenzene: 0.3 ppm, Lead: 70 ppm, Mercury: 0.50 ppm, Methylene chloride: 37.5 ppm, Nickel: 6.80 ppm, Phenol: 29.0 ppm, Tetrachloroethylene: 3.40 ppm, Toluene: 7.0 ppm, 1,1,1-Trichloroethane: 2.0 ppm, Trichloroethylen: 6.50 ppm, Xylenes: 1.60 ppm Target concentrations: 375 ppm Calculated consumption in high dose group in µg/mouse/day: Acetone: 131, Aroclor 1260, Arsenic 28.1, Benzene 37.6, Cadmium 152, Carbon tetrachloride 1.02, Chloroform 19.3, Chlorobenzene 0.32, Chromium 107, 1,1-Dichloroethane 4.29, 1,1-Dichloroethylene 1.35, 1,2-Dichloroethane 104, 1,2-t-Dichloroethylene 7.73, Di/2-ethylhexyl)phthalate, Ethylbenzene 1.06, Lead , Mercury 1.35, Methylene chloride 102, Nickel 18.6, Phenol 86.4, Tetrachloroethylene 9.04, Toluene 21.6, 1,1,1-Trichloroethane 6.37, Trichloroethylen 21.8, Xylenes 4.35
How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?)	Would have to be evaluated, NOAELs of individual compounds are not given.
No. of technical replicates per exposure condition (*in vitro*)	not applicable
No. of animals per dose group (*in vivo*)	8 mice/group
Observations/Findings	Mid and high dose: Increased relative Kidney weights, no other changes observed.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Good study, sufficient animal numbers.