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
In vivo **Study Type**	
Route of Administration	drinking water, water control group
Species & age of animals	F344/N rats, 6 weeks
Study Duration	26-weeks
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	body weight, mortality, organ weights, histopathology, clinical pathology, neurobehaviour (grip strengths of fore- and hindlimbs, hindlimb footsplay, horizontal and vertical activity counts, pawlick latency, startle response investigated in weeks 6, 12, 18, 24), reproductive toxicity
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 four dose levels were administered
Were no effect levels established?	Yes
Were doses below the NO(A)ELs investigated?	Yes presumably
Mixtures Investigated	Target concentrations: Acetone: 1.59, 5.3, 15.9, 53 ppm, Aroclor 1260: 0.0003, 0.001, 0.003, 0.01 ppm, Arsenic: 0.27, 0.9, 2.7, 9.0 ppm, Benzene: 0.375, 1.25, 3.75, 12.5 ppm, Cadmium: 1.53, 5.1, 15.3, 51.0 ppm, Carbon tetrachloride: 0.012, 0.04, 0.12, 0.40 ppm, Chloroform: 0.21, 0.7, 2.1, 7.0 ppm, Chlorobenzene: 0.003, 0.01, 0.03, 0.10 ppm, Chromium: 1.08, 3.6, 10.8, 36.0 ppm 1,1-Dichloroethane: 0.042, 0.14, 0.42, 1.4 ppm, 1,1-Dichloroethylene: 0.015, 0.05, 0.15, 0.5 ppm, 1,2-Dichloroethane: 1.2, 4.0, 12, 40.0 ppm, 1,2-t-Dichloroethylene: 0.075, 0.25, 0.75, 2.5 ppm, Di-2-ethylhexyl)-phthalate: 0.0005, 0.0015, 0.0045, 0.015 ppm, Ethylbenzene: 0.009, 0.03, 0.09, 0.3 ppm, Lead: 2.1, 7.0, 21, 70.0 ppm, Mercury: 0.017, 0.05, 0.17, 0.50 ppm, Methylene chloride: 1.125, 3.75, 11.25, 37.5 ppm, Nickel: 0.204, 0.68, 2.04, 6.80 ppm, Phenol: 0.87, 2.9, 8.7, 29.0 ppm, Tetrachloroethylene: 0.102, 0.34, 1.02, 3.40 ppm, Toluene: 0.21, 0.7, 2.1, 7.0 ppm, 1,1,1-Trichloroethane: 0.06, 0.2, 0.6, 2.0 ppm, Trichloroethylen: 0.195, 0.65, 1.95, 6.50 ppm, Xylenes: 0.048, 0.16, 0.48, 1.60 ppm Total concentrations: 11.3428, 37.8025, 113.128, 378.025 ppm
Number of dose levels	Two mixtures tested, of which one was below the NOEL for both components individually
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*)	20 rats/sex/group neurobehavioural paramter investigated in 10 rats/sex/group
Observations/Findings	High dose body weight gain↓ (males only), abs. and rel. Liver weights ↑, abs. and rel. Kidney weights ↑(in males rel. Weights only), microcytic anemia with iron depletion, multiple foci of inflammation, bile duct and oval cell hyperplasia (females only), mesenteric lymph node, adrenal and spleen hyperplasia, hemosiderin in spleen ↓ Neurobehavioural changes: no treatment-related changes observed in all dose groups
Overall opinion	
(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; NOAELs of individual compounds should be evaluated and compared to the actual doses administered.