

Guidelines/Criteria	
References:	<p>Jadhav SH, Sarkar SN, Aggarwal M, Tripathi HC. 2007a. Induction of oxidative stress in erythrocytes of male rats subchronically exposed to a mixture of eight metals found as groundwater contaminants in different parts of India. Arch Environ Contam Toxicol 52:145-151.</p> <p>Jadhav SH, Sarkar SN, Patil RD, Tripathi HC. 2007b. Effects of subchronic exposure via drinking water to a mixture of eight water-contaminating metals: A biochemical and histopathological study in male rats. Arch Environ Contam Toxicol 53:667-677.</p>
In vivo Study Type Route of Administration Species & age of animals	drinking water male Wistar rats,
Study Duration	90 day study
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	no yes dissimilar action assumed repeated dose toxicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	organ weights (brain, heart, liver, kidney, lungs, testes), histopathology, clinical chemistry, Blood sampling (after 30, 60, 90 days), Adverse
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?	No Concentrations given are in ppm: MPL, 1x, 10x, 100x: Sodium arsenite 0.096, 0.38, 3.8, 38.0; Calcium chloride 0.005, 0.098, 0.98, 9.8; lead acetate 0.018, 0.220, 2.20, 22.0, mercuric chloride 0.008, 0.06, 0.6, 6.0, chromium trioxide 0.141, 0.346, 3.46, 34.6, nickel chloride 0.081, 0.810, 8.10, 81.0, manganese chloride 1.800, 2.026, 20.26, 202.6, ferric chloride 0.870, 2.033, 20.33, 203.3 No, only mixtures at different concentrations tested No Presumably as lowest concentration represents WHO MPLs
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 (<i>in vitro</i>) No. of animals per dose group (<i>in vivo</i>)	MPLs, and 3 dose levels (1x, 10x, 100x) representative of groundwater contamination of different areas of India MPLs, 1x, 10x, 100x of environmental concentrations were tested. Highest concentrations detected in Indian groundwater were: sodium arsenite: 3.71, cadmium chloride: 1.00, lead acetate 38.25, mercuric chloride 1.36, chromium trioxide 4.88, nickel chloride 1.87, manganese chloride 6.24, ferric chloride 32.26 not applicable 10 animals/group
Observations/Findings	MPL, 1x: no organ weight changes ≥ 10x: decreased body weights, decreased water consumption, increased relative brain weight, increased absolute and relative kidney weight, increased relative liver weights. 100x: increased absolute brain weight; statistically significant histomorphological changes in kidney (vascular engorgement, extravasation of erythrocytes, hyaline cast formation and karyomegaly in renal tubules, and glomerular dilatation, vacuolar degeneration and diffuse necrosis of tubular epithelial cells and focal infiltration of mononuclear cells around glomerulus), liver (vascular engorgement, extravasation of erythrocytes, infiltration of mononuclear cells, degeneration and necrosis of hepatocytes), and brain (vascular engorgement, occasional haemorrhages, satellitosis in cerebral cortex, focal gliosis around the degenerating neurons).
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Sufficient number of animals. Adequate documentation and study design.