Reinstein et al, 1984

Guidelines/Criteria	
Reference:	Reinstein NH, Lönnerdal B, Keen CL, Hurley LS. 1984. Zinc-copper interactions in the pregnant rat: fetal outcome and maternal and fetal zinc, copper and iron. J Nutr 114(7):1266-1279.
In vivo **Study Type** Route of Administration Species & age of animals	 in the diet pregnant SD rats, no age given, wieghthon the day of delivery 190-200g
Study Duration	three weeks (Day 0-21 of gestation)
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 yes dissimilar acting ? general toxicity, repro-toxicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	 Maternal food intake, maternal weight gain, foetal weight, no. of litters, no. of rats with resorptions, no of implantations sites, total resorptions, total live foetuses, malformed foetuses, and of malformations. maternal haematocrit, haemoglobin, total plasma cholesterol and plasma triglycerides adverse effects
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 data zinc, copper no yes only in part, i.e., not for all compounds
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 (*in vitro*) No. of animals per dose group (*in vivo*)	 one (zinc) or 2 (copper) 1xNOAEL Zn & 1/19xNOAEL Cu, NOAEL Zn & 1xNOAEL Cu at least seven
Observations/Findings	No effects on general and repro-toxicity at all. A proper statistical evaluation of clinico-chemical parameters was not provided. These data were not considered.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	 Complex nutritional design, groups with deficient amounts of Zn an Cu were not considered. Control group contains "normal " amounts of Zn and Cu. No dose response. Statistic evaluation of clinico-chemical parameters in our sense not available. In comparison to modern standards, low number of animals. No indication of combination effect for general toxicity and repro-toxicity. Data of general and repro-toxicity fit to our criteria, clinical chemistry cannot be evaluated.