Mayura et al, 1984

Guidelines/Criteria	
Reference:	Mayura K, Parker R, Berndt WO, Phillips TD. 1984. Effect of simultaneous prenatal exposure to ochratoxin A and citrinin in the rat. J Toxicol Environ Health 13:553-561.
In vivo **Study Type** Route of Administration Species & age of animals	Single dose rat teratogenicity study (dosed either on day 5, 6, 7, 8, 10, 11 or 14 of gestation) Subcutaneous Sprague-Dawley rats
Study Duration	gestation
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Yes Possibly (both potent teratogens and nephrotoxins, both mycotoxins)
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	 Maternal body weight, number of implants, resorptions, live foetuses, foetal body weight and foetal abnormalities of many kinds 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?	 Ochratoxin A and citrinin Yes 1mg/kg for ochratoxin, 30mg/kg for citrinin, for all dosing days. The authors report other work showing 1.75mg/kg of ochratoxin and 35mg/kg of citrinin to be teratogenic as single doses in rats. No
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*)	 1 One, 1mg/kg of ochratoxin and 30mg/kg for citrinin, i.e. the single component NOELs, tested at each dosing day 6-10 litters per group, mainly 7
Observations/Findings	The mixture caused an increase in resorptions and reduction in live foetuses which reached significance when dosed on days 5 and 7 (plus reduction in implants when dosed on day 7). The mixture caused significantly increased malformations at most dose timings, including rib abnormalities, hydronephrosis, hydrocephaly and spinal defects. Though the single compounds increased skeletal malformations it didn't reach statistical significance.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	A reasonable study, though more replication of the controls or use of historical control data would have been helpful. Lack of lower doses is a limitation.