Sansing et al, 1976

Guidelines/Criteria	
Reference:	Sansing GA, Lillehoj EB, Detroy RW, Miller MA. 1976. Synergistic toxic effects of citrinin, ochratoxin A and penicillic acid in mice. Toxicon 14:213-220.
***In vivo* Study Type** Route of Administration Species & age of animals	Single dose lethality study IP Female CD1 25g mice
Study Duration	72hrs
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	 Yes No Possibly, all three mycotoxins are hepatotoxins and nephrotoxins. Nothing specific
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	 Death 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?	 Citrinin, ochratoxin A and penicillic acid Yes 25mg/kg for citrinin, 6.2mg/kg for ochratoxin, 25mg/kg for penicillic acid. 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*)	 4 dose levels of each of 4 different ratios of each pair of mycotoxins Four different ratios of components used 6
Observations/Findings	Either two or three dose levels for each mixture were at single-component effect levels, meaning only one or two were at NOELs. Of the 18 groups dosed at or below the NOELs for each component, 16 resulted in no lethalities, whilst two resulted in a single mortality each: 20mg/kg citrinin + 3.8 mg/kg ochratoxin A (0.8x NOEL + 0.62x NOEL); 20mg/kg citrinin + 0.6 mg/kg ochratoxin A (0.8x NOEL + 0.1x NOEL).
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	A reasonable study which was supplemented with investigation of the incorporation of radiolabelled orotic acid into liver and kidney - an early marker of tissue damage/repair. This showed that each component at its NOEL affected this marker, but no histopathology was conducted. Main limitation is the crude nature of lethality as an endpoint.